Received: 30 October 2024 | Revised: 27 January 2025 | Accepted: 14 February 2025

DOI: 10.1111/aogs.15088

ORIGINAL RESEARCH

Maternal time interval between menarche and childbirth is associated with daughter's age at menarche

Mari Landås Warp[1,2,3] | Thea Grindstad[2] | Karoline H. Skåra[2] | Maria C. Magnus[2] | Siri E. Håberg[2,4] | Nils-Halvdan Morken[2,3,5] | Liv Bente Romundstad[2,6] | Cecilia H. Ramlau-Hansen[7] | Hans Ivar Hanevik[1,2]

[1]Telemark Hospital Trust, Fertilitetsavdelingen Sør, Porsgrunn, Norway

[2]Centre for Fertility and Health, Norwegian Institute of Public Health, Oslo, Norway

[3]Department of Clinical Science, University of Bergen, Bergen, Norway

[4]Department of Global Public Health and Primary Care, University of Bergen, Bergen, Norway

[5]Department of Obstetrics and Gynecology, Haukeland University Hospital, Bergen, Norway

[6]Volvat Spiren Fertility Clinic, Trondheim, Norway

[7]Department of Public Health, Aarhus University, Aarhus, Denmark

Correspondence
Mari Landås Warp, Telemark Hospital Trust, Fertilitetsavdelingen Soer, Aallsgate 41, Porsgrunn 3710, Norway.
Email: marilandas.warp@fhi.no

Funding information
European Research Council, Grant/Award Number: 101071773; Norges Forskningsråd, Grant/Award Number: 320656 and 262700; H2020 European Research Council, Grant/Award Number: 947684

Abstract

Introduction: Women's reproductive lifespan has increased over the past two decades. Simultaneously, female reproductive behavior has changed, with increasing age at first birth. Early menarche has been associated with adverse health outcomes, but research investigating the association between maternal age at childbirth and daughter's age at menarche is, so far, inconclusive. Whether the interval between menarche and childbirth or between childbirth and menopause among mothers is associated with age at menarche in daughters is not known.

Material and Methods: We conducted a cohort study with retrospectively collected data including mothers and daughters participating in the Norwegian Mother, Father and Child Cohort Study. Within this cohort, we identified two study populations. First, we included 14 576 mother-daughter pairs with complete information on maternal age at menarche and childbirth and the daughter's age at menarche. Second, we included 1350 mother-daughter pairs with complete information on maternal age at childbirth and natural menopause, and daughter's age at menarche. We calculated odds ratios (OR) with 95% confidence intervals (CIs) in a discrete survival analysis for daughters' age at menarche by time intervals from menarche to childbirth or from childbirth to menopause in mothers. We adjusted for relevant covariates.

Results: We found 5% lower yearly odds (partially adjusted OR 0.95 (CI 0.90–0.99)) of reaching menarche among daughters born by mothers <16 years after menarche compared to the reference category born 16–20 years following menarche. After additionally adjusting for maternal birth year, the effect estimate was further reduced (fully adjusted OR 0.79 (CI 0.74–0.84)). Among daughters born by mothers >20 years after menarche, the likelihood of early menarche was higher (fully adjusted OR 1.19 (CI 1.13–1.27)) compared to the reference category. Regarding the childbirth-menopause interval, our findings did not reach statistical significance in either of our models.

Abbreviations: BMI, body mass index; CI, confidence interval; MoBa, Norwegian Mother, Father and Child Cohort Study; OR, odds ratio.

Conclusions: Daughters born to mothers with a shorter time interval (<16 years) between menarche and childbirth have a lower likelihood of experiencing early menarche compared to the reference category (16–20 years), and daughters born to mothers with a longer time interval from menarche to childbirth (>20 years) have a higher likelihood of reaching early menarche.

KEYWORDS
age at childbirth, age at menarche, age at menopause, father and child cohort study, MoBa, reproductive lifespan

1 | INTRODUCTION

A woman's reproductive lifespan starts at menarche and ends at menopause. The interval between these two events has, on average, increased in duration over the last decades.[1,2] Decreasing age at menarche is also seen in Norway, with a mean age at menarche of 12.9 years in 2020 compared to 13.3 years in 2006.[3] A concurrent increase in age at menopause has also taken place, as the mean age was 50.3 years for Norwegian women born in the 1930s and 52.7 years for those born in the 1960s.[1] Female reproductive behavior has also changed in recent decades, notably with older age at first childbirth.[4] The mean age at first birth in Norwegian mothers was 30.3 years in 2023, an increase from 26.0 years in 1993.[5]

Early menarche (<11 years) is associated with adverse health outcomes such as reduced fecundability and a higher risk of cardiovascular disease and breast cancer.[6–8] Since the age at menarche keeps declining, the identification of modifiable risk factors and predictors of age at menarche is important.[9] To date, the most accurate predictor of a daughter's age at menarche is the age at menarche in her mother, and the same applies to menopause where heritability for these events is around 25%–50%.[10–13] Environmental factors such as high body mass index (BMI), exposure to cigarette smoking in utero, and paternal absence in childhood have also been associated with early menarche in some studies.[14–16] The association between maternal age at childbirth and age at menarche in the offspring was addressed in two previous studies.[17,18] Thomsen and co-authors found no association, while Shrestha and co-workers found a slightly reduced age at menarche with increasing maternal age at childbirth. Neither of these studies included maternal reproductive lifespan in their analyses. This is an important omission since a woman who gives birth at 30 years of age could have a long or short interval from menarche to childbirth, and similarly, a long or short interval from childbirth to menopause.

Variation in the menarche-childbirth interval affects the duration of the post-pubertal ovary's exposures to different environmental factors such as endocrine disruptive chemicals (EDCs) and cigarette smoke.[19] Environmental exposures may influence a woman's oocytes, and the accumulated exposure level before pregnancy could in turn affect the developing oocytes in her daughter during fetal development.[20,21] Similarly, the time left to menopause for women who give birth at 30 years of age varies between individuals, and although female chronological age is associated with ovarian age, they are not identical measures of aging.[22] The childbirth-menopause interval is mainly determined by the number of oocytes a woman has left in her ovaries at the time of giving birth and the rate of depletion of this ovarian reserve after childbirth. Both factors show considerable inter-individual variation,[23] and it is hypothesized that maternal ovarian age at pregnancy may have effects on the daughter's oocyte pool,[20] which again can be associated with age at menarche.

Key message

Early menarche is associated with negative health outcomes, and investigating preventive measures is of importance. In this study, we found that mothers who give birth shortly after their own menarche have daughters with a reduced likelihood of early menarche.

To increase the understanding of maternal influences on their daughters' age at menarche, a more complete perspective might result from investigating the time interval between the maternal reproductive milestones of menarche and menopause in addition to maternal chronological age at childbirth. Currently, studies investigating these associations are lacking. Here we investigate whether intervals between menarche and childbirth, or childbirth and menopause, in mothers are associated with age at menarche in daughters.

2 | MATERIAL AND METHODS

2.1 | Study population

The Norwegian Mother, Father, and Child Cohort Study (MoBa) is a cohort study conducted by the Norwegian Institute of Public Health. In this population-based pregnancy cohort, pregnant women from across Norway were invited, and 41% of the invited women took part in the study.[24] The recruitment period was between 1999 and 2008,

and about 95 200 mothers, 75 200 fathers, and 114 500 children were included. Women in MoBa could either be nulliparous or parous at baseline. Additionally, if they became pregnant multiple times during the inclusion period, they were eligible to participate with subsequent pregnancies. We defined two separate study populations (Figure 1). In the first study population, we included MoBa mothers with information on their menarche-childbirth interval and daughters' age at menarche ($N = 14\,576$). In the second study population, we included MoBa

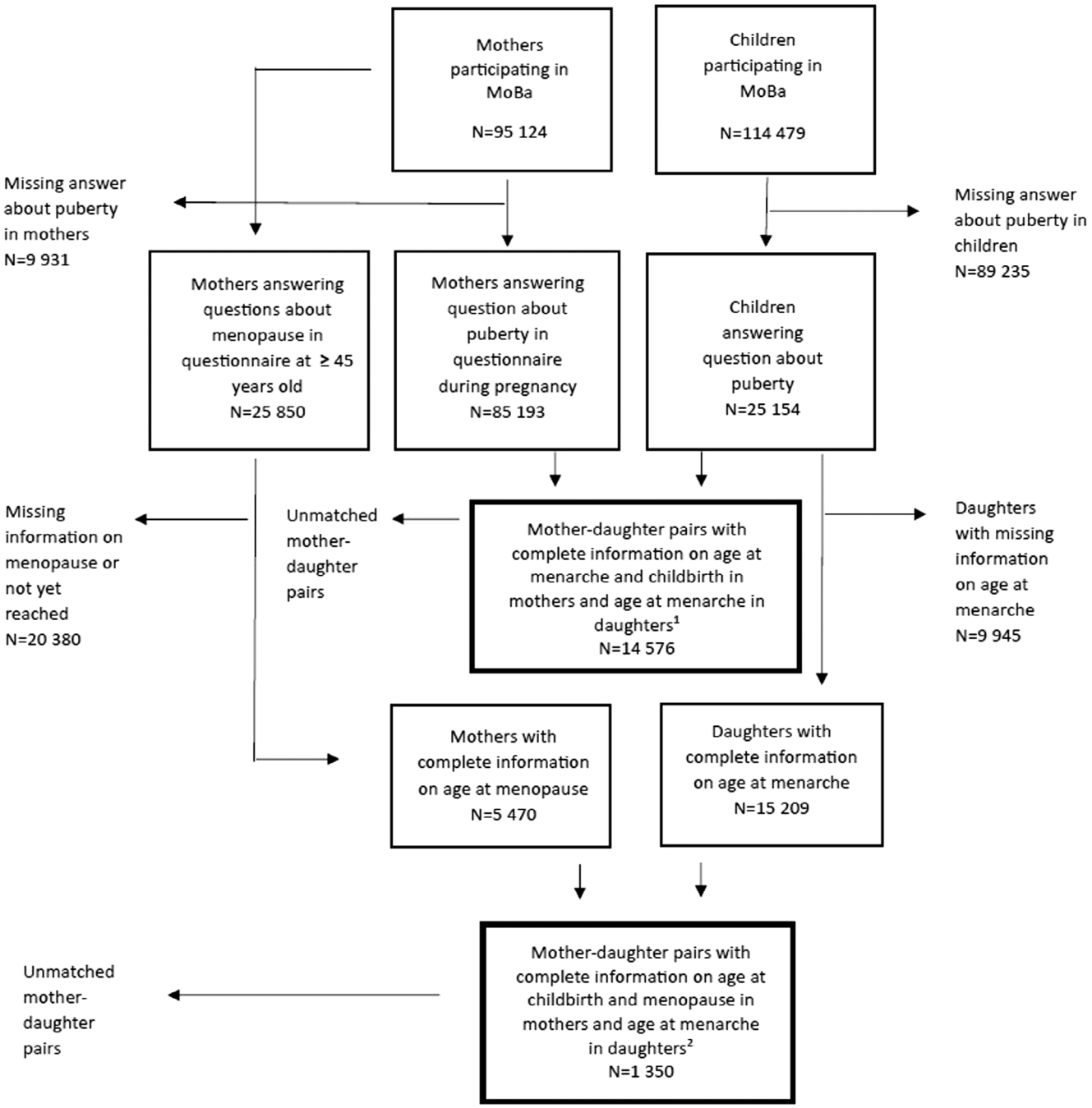

FIGURE 1 Flow chart of participants included in our study based on the Norwegian Mother Father and Child Cohort Study (MoBa). [a]14 576 mother-daughter pairs with complete data on the exposure (maternal menarche-childbirth interval) and outcome (daughter's age at menarche). The mothers' age at menarche was obtained from a questionnaire completed during pregnancy, while the age at childbirth was sourced from the Medical Birth Registry of Norway. Their daughters' age at menarche was collected from questionnaires submitted at ≥14 years old, and if the question about menarche was not answered or not yet reached menarche, information was gathered from questionnaires submitted ≥18 years old. [b]1350 mother-daughter pairs with complete data on the exposure (maternal childbirth-menopause interval) and outcome (daughter's age at menarche). Age at childbirth was sourced from the Medical Birth Registry of Norway. Information on age at menopause was gathered from a questionnaire submitted at ≥45 years old. Their daughters' age at menarche was collected from questionnaires submitted at ≥14 years old, and if the question about menarche was not answered or if menarche had not yet been reached information was gathered from questionnaires submitted at ≥18 years old.

mothers with information on the childbirth-menopause interval and daughters' age at menarche ($N = 1350$).

2.2 | Maternal menarche-childbirth and childbirth-menopause intervals

The first MoBa questionnaire was handed out at recruitment and asked the MoBa mothers to provide their age (in whole years) at their first menstruation. Information on whether the MoBa mothers had experienced a period in the past year, the main reason for not having had a period, and the year and month of their last period was obtained through a follow-up questionnaire administered to all MoBa mothers who had reached 45 years or older. Natural menopause was defined as not having menstruated in the past 12 months due to menopause. Information about the mothers' age at delivery was obtained from the Medical Birth Registry of Norway (MBRN) which contains information about all births in Norway.

The interval between maternal menarche and the birth of her daughter in the study was calculated by subtracting age (in years) at maternal menarche from age at childbirth. Similarly, the interval between childbirth and natural menopause was calculated by subtracting age (in years) at childbirth from age at menopause.

2.3 | Age at menarche in MoBa daughters

Daughters in MoBa were asked to indicate when they got their first menstrual period in whole years through questionnaires administered to all MoBa offspring when they were 14 and 18 years of age. We also collected information about age at menarche from MoBa daughters between 18 and 22 years participating in a substudy. If the daughters had given their age at menarche in multiple questionnaires, we included their answer the first time they reported age at menarche to minimize recall bias.

2.4 | Covariates

We selected potential confounding factors a priori (Figure S1) and adjusted for various maternal characteristics (pre-pregnancy BMI, highest completed or ongoing education level as proxy for socioeconomic status, and cigarette smoking during pregnancy). To avoid bias from age effects and temporal trends, we also adjusted for maternal age at menarche and maternal birth year (whole years; continuous).

Self-reported information on height and pre-pregnancy weight (used to calculate BMI; continuous), mothers' highest completed or ongoing education level (<high school/high school/up to 4 years of college/>4 years of college) and smoking status during pregnancy (yes/no) was collected from mothers through a questionnaire at recruitment. Information about maternal age at childbirth was collected from the MBRN.

2.5 | Statistical analyses

We conducted a discrete-time survival analysis using a complementary log–log link function to study the time until daughters' age at menarche. We used daughters' age at menarche as the unit of time starting at 9 years and censoring after 18 years. We ran two main analyses with the duration of the two maternal reproductive intervals as exposures.

In the first analysis, the exposure was the time interval in years from maternal menarche to childbirth. We divided the menarche-childbirth interval into three categories according to the <25th percentile, 25–75 percentile, and >75th percentile: <16 years, 16–20 years (reference) and >20 years. In the second analysis, the exposure was the time interval in years from maternal childbirth to menopause. We divided the childbirth-menopause interval into three categories based on the <25th percentile, 25–75 percentile, and >75th percentile: <12 years, 12–15 years (reference) and >15 years. The effect estimates for both analyses are expressed as odds ratios (ORs) representing the daughter's yearly likelihood of reaching menarche compared to the reference category. An OR <1 indicates a lower yearly likelihood of reaching menarche compared to the reference category.

The multivariable models adjusted for maternal age at menarche, highest completed or ongoing education level as a proxy for socioeconomic status, pre-pregnancy BMI, and maternal cigarette smoking during pregnancy. A second model further adjusted for maternal birth year.

2.6 | Additional analyses

We conducted a stratified analysis to assess the robustness of our findings. Using the menarche-childbirth interval as exposure, we checked if associations were similar for different categories of maternal age at menarche (<12 years, 12–14 years and >14 years). The three strata are according to the 25th and 75th percentiles. We adjusted for maternal highest completed or ongoing education level, pre-pregnancy BMI, and cigarette smoking during pregnancy, and a second model additionally adjusted for maternal birth year.

To supplement our findings, we further explored whether maternal age at childbirth was associated with daughters' age at menarche ($N = 14\,576$). This was done since previous studies showed conflicting findings in this regard. Exposure categories for maternal age at childbirth were created according to the 25th and 75th percentiles (<29 years, 29–33 years (reference) and >33 years). Herein, we adjusted for maternal age at menarche, highest completed or ongoing education level, pre-pregnancy BMI, and cigarette smoking during pregnancy, and additionally for maternal birth year in a second model.

Since previous studies show a strong association between age at menarche in mothers and daughters, we explored if this association also was present in our dataset ($N = 14\,576$). Exposure categories for maternal age at menarche were created according to the 25th and 75th percentiles (<12 years, 12–14 years (reference) and >14 years). Daughters' age at menarche was used as the outcome to assess if early menarche in mothers was associated with higher

odds of early menarche in daughters and if late menarche in mothers was associated with lower odds of early menarche in daughters. We adjusted for maternal characteristics such as the highest completed or ongoing education level, pre-pregnancy BMI, cigarette smoking during pregnancy, and additionally for maternal birth year in a second model.

The maternal use of assisted reproductive technology (ART) to conceive was in one large study associated with early menarche in daughters.[25] To explore this effect on the mode of conception in our dataset, we ran a sensitivity analysis restricted to those participants that conceived without ART. The exposure categories and adjusted variables were the same as in the main analyses.

All analyses were conducted in STATA version 17 (Stata Corp, Texas).

3 | RESULTS

Table 1 shows background characteristics according to maternal reproductive intervals. Figure 2 shows the distributions of age at menarche for both mothers and daughters, and age at childbirth and menopause for all mothers included. Age at menarche among mothers and daughters was normally distributed ranging from 8 to 21 years, with a mean of 12.6 (SD 1.1) years among daughters, which was four months earlier than their mothers who reported a mean age at menarche of 13.0 (SD 1.4) years. Only 0.6% of all daughters and 3.4% of mothers reported an age at menarche ≥16 years. The mean age at childbirth among mothers was 31.6 (SD 4.4) years, while the median age at natural menopause was 50 years, and 81.4% of women ($N = 1099$) reported an age at menopause between 45 and 55 years.

TABLE 1 Background characteristics for mothers with available data on two reproductive intervals: Menarche-childbirth ($N = 14\,576$) and childbirth-menopause interval ($N = 1350$).

	Menarche-childbirth interval ($n = 14\,576$)		Childbirth-menopause interval ($n = 1350$)	
	Participants	Missing	Participants	Missing
Maternal characteristics	*n* (%)	*n* (%)	*n* (%)	*n* (%)
Age at menarche	14 576 (100)	0 (0)	n/a	n/a
<12	1735 (11.9)			
12–14	11 031 (75.7)			
>14	1810 (12.4)			
Age at childbirth	14 576 (100)	0 (0)	1350 (100)	0 (0)
<29	4595 (31.6)		23 (1.7)	
29–33	6170 (42.3)		331 (24.5)	
>33	3811 (26.1)		996 (73.8)	
Age at menopause[a]	n/a	n/a	1350 (100)	0 (0)
<50 years			659 (49.0)	
50–52 years			469 (34.7)	
>52 years			222 (16.4)	
Pre-pregnancy BMI	14 231 (97.6)	345 (2.3)	1302 (96.5)	48 (3.5)
<18.5	386 (2.7)		21 (1.6)	
18.5–24.9	9423 (66.2)		886 (68.0)	
25–29.9	3145 (22.1)		276 (21.2)	
>30	1277 (9.0)		119 (9.1)	
Education level	14 515 (99.6)	61 (0.4)	1325 (98.2)	25 (1.8)
<High school	576 (4.0)		40 (3.0)	
High school	3283 (22.6)		296 (22.3)	
Up to 4 years college	6631 (45.7)		579 (43.7)	
>4 years of college	4025 (27.7)		410 (31.0)	
Smoking during pregnancy[b]	12 597 (86.4)	1979 (13.6)	1084 (80.3)	266 (19.7)
No	11 598 (92.1)		975 (90.0)	
Yes	999 (7.9)		109 (10.0)	

[a]Menopause was identified in those who answered that they had not been menstruating for the past 12 months, indicated their last menstrual period (year), and indicated that the cause of not menstruating was menopause.

[b]Smoking during pregnancy. Yes: sometimes or daily. No: never.

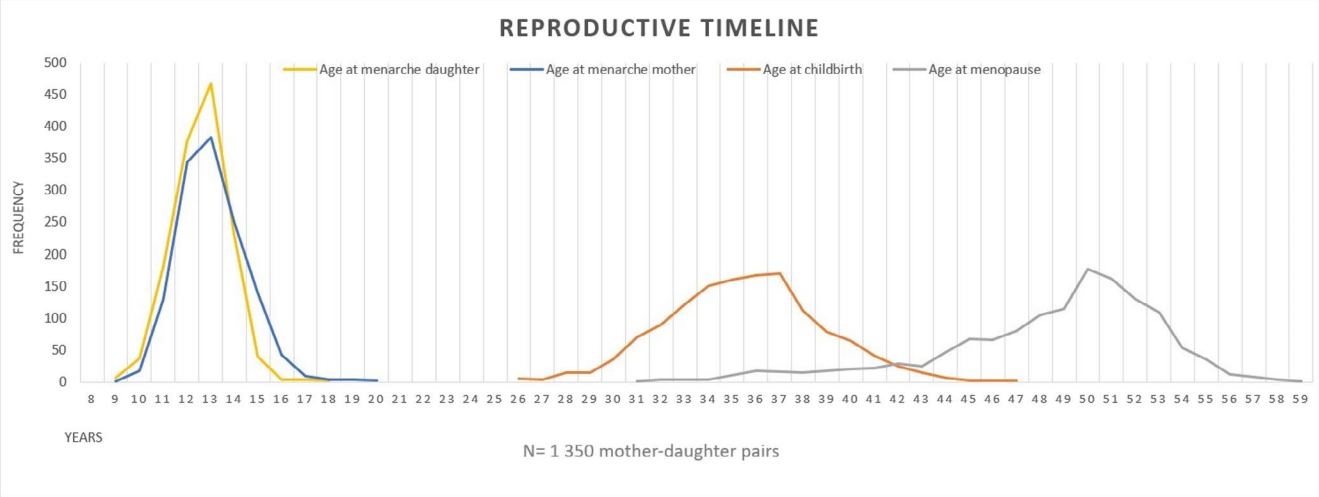

FIGURE 2 Distribution of age at menarche (for both mothers and daughters), age at childbirth and age at menopause for all mothers included in our dataset (*N* = 1350). Mean age at menarche daughters (12.6, SD 1.1), mothers (13.0, SD 1.4), mean age at menopause mothers (48.4, SD 4.6), mean age at childbirth mothers (35.5, SD 3.2), mean interval between menarche-childbirth (22.5, SD 3.2), mean interval between childbirth and menopause (12.8, SD 4.8).

TABLE 2 Daughters' yearly odds of reaching menarche by categories of maternal menarche-childbirth interval (*N* = 14 576) and childbirth-menopause interval (*N* = 1350).

	Menarche-childbirth interval			Childbirth-menopause interval		
Category	**<16**	**16–20 (Reference)**	**>20**	**<12**	**12–15 (Reference)**	**>15**
n	4662	6030	3884	388	508	454
Crude OR (95% CI)	0.90 (0.87–0.94)	1	1.09 (1.04–1.13)	1.04 (0.91–1.20)	1	0.88 (0.77–1.01)
Model 1 OR (95% CI)	0.95 (0.90–0.99)	1	1.00 (0.95–1.04)	1.02 (0.87–1.19)	1	0.88 (0.75–1.03)
Model 2 OR (95% CI)	0.79 (0.74–0.84)	1	1.19 (1.13–1.27)	1.05 (0.90–1.23)	1	0.88 (0.75–1.03)

Note: Crude and adjusted odds ratios (OR's) with 95% confidence intervals (CIs). Menarche-childbirth interval: Model 1 adjusted for maternal age at menarche, maternal pre-pregnancy body mass index (BMI), maternal highest completed or ongoing education level as proxy for socioeconomic status and maternal cigarette smoking during pregnancy. Model 2 adjusted for maternal age at menarche, maternal pre-pregnancy BMI, maternal highest completed or ongoing education level, maternal cigarette smoking during pregnancy and maternal birth year. Childbirth-menopause interval: Model 1 adjusted for maternal age at menarche, maternal pre-pregnancy BMI and maternal highest completed or ongoing education level as proxy for socioeconomic status and maternal cigarette smoking during pregnancy. Model 2 adjusted for maternal age at menarche, maternal pre-pregnancy BMI, maternal highest completed or ongoing education level as proxy for socioeconomic status maternal cigarette smoking during pregnancy and maternal birth year.

3.1 | Maternal menarche-childbirth interval and daughter's age at menarche (*N* = 14 576)

The menarche-childbirth interval ranged from 3 to 34 years with a median of 18 years. Table S1A shows the maternal background characteristics by interval from menarche to childbirth. Table 2 shows the association between the menarche-childbirth interval in mothers and age at menarche in daughters. A short (<16 years) interval was associated with a 5% lower yearly odds of daughters' reaching menarche compared to the reference interval of 16–20 years after adjusting for maternal age at menarche, highest completed or ongoing education level, maternal pre-pregnancy BMI, and maternal cigarette smoking during pregnancy (OR 0.95 (CI 0.90–0.99)). Additional adjustment for maternal birth year had a clear impact on the effect estimate (OR 0.79 (CI 0.74–0.84)). A long (>20 years) menarche-childbirth interval was not associated with daughter's age at menarche in our partially adjusted model compared to daughters born 16–20 years after menarche. However, when additionally adjusting for maternal birth year, we found a 19% higher yearly odds of reaching menarche compared to the reference category (OR 1.19 (CI 1.13–1.27)).

3.2 | Maternal childbirth-menopause interval and daughter's age at menarche (*N* = 1350)

The time interval from childbirth to menopause ranged from 0 to 23 years with a median of 14 years. Table S1B shows the maternal

background characteristics by interval from childbirth to menopause. Table 2 shows the association between the childbirth-menopause interval in mothers and age at menarche in daughters. Among daughters born by mothers with >15 years left until menopause, we observed a 12% lower yearly odds (OR 0.88 (CI 0.75–1.03)) of reaching menarche compared to the daughters born by mothers in the reference category of 12–15 years, although this association did not reach statistical significance. We adjusted for maternal age at menarche, highest completed or ongoing education level, maternal pre-pregnancy BMI, and smoking status during pregnancy. When additionally adjusting for maternal birth year, the association remained identical (OR 0.88 (CI 0.75–1.03)). No association with daughters' age at menarche was detected in mothers who gave birth with few years (<12) left of their reproductive lifespan when comparing to the reference category in either of our adjusted models.

3.3 | Additional analyses

In our stratified analyses, we found that among daughters born by mothers with a normal age at menarche (12–14 years), those born <16 years after maternal menarche had 10% lower yearly odds of reaching menarche compared to those born between 16 and 20 years after maternal menarche (Table S2). After additionally adjusting for maternal birth year, the effect increased (OR 0.72 (CI 0.67–0.77)). Regarding mothers with early (<12 years) or late (<14 years) menarche, their menarche-childbirth interval was not associated with the daughter's age at menarche in the partially adjusted model. However, after additionally adjusting for maternal birth year, an association was detected (<12 years: OR 0.88 (CI 0.86–0.95) and >14 years: OR 0.73 (CI 0.62–0.86)). We found in our fully adjusted model that among daughters born by mothers with a normal age at menarche (12–14 years), those born >20 years after maternal menarche had a higher yearly odds of reaching menarche compared to those born between 16 and 20 years after maternal menarche (OR 1.27 (CI 1.19–1.36)).

We observed a strong association between both early and late menarche among mothers and the odds of early and late menarche in daughters (Table S3). The results were similar across crude and adjusted models. We found that daughters born to mothers with early menarche (<12 years) had 60% higher yearly odds of reaching menarche compared to daughters born to mothers who reached menarche between 12 and 14 years. Daughters born to mothers with late menarche (>14 years) had a 26% lower yearly odds of reaching menarche compared to the reference category.

Using age at childbirth in mothers as exposure (<29 years, 29–33 years (reference) and >33 years) and age at menarche in daughters as outcome, no association was detected in our partially adjusted model (Table S4). After additionally adjusting for maternal birth year, we found lower early odds of reaching menarche among daughters born by younger mothers (<29 years) and higher yearly odds of reaching menarche among older mothers (>33 years), compared to the reference category of mothers aged 29–33 years.

Restricting the study population to mothers that conceived without ART decreased the number of participants in the menarche-childbirth interval by 387 ($N = 14\,789$), and the number of participants in the childbirth-menopause interval by 67 ($N = 1283$). As shown in Table S5, this did not alter the results noticeably.

4 | DISCUSSION

In this population-based cohort, we found that a shorter maternal time interval (<16 years) from menarche to childbirth was associated with a lower yearly odds of reaching menarche in daughters, and a longer maternal time interval (>20 years) was associated with higher yearly odds of reaching menarche in daughters compared to the reference category (16–20 years). We also found an association between a longer maternal time interval (>15 years) from childbirth to menopause and lower yearly odds of reaching menarche in daughters, but this association was not statistically significant.

Despite extensive research efforts, the biological mechanisms that underpin the initiation of female puberty are not well understood, and hundreds of genes have been associated with the timing of menarche.[12] Nevertheless, ovarian physiology is undoubtedly a cornerstone in female pubertal development.[26] It is estimated that females are born with 1–2 million oocytes, and the decline of the ovarian reserve occurs at different rates throughout women's lifespan until menopause when the oocyte pool is virtually empty.[26] Recent data show that the follicular dynamics in the premenarcheal ovary vary between individuals[27] and animal studies have indicated that the size of the oocyte pool is likely to be determined during embryonic development.[28]

Our results indicate a reduced likelihood of undergoing early menarche in daughters when the mothers gave birth <16 years after their own menarche. One possible explanation for this could be that the maternal post-pubertal ovary has had a shorter exposure window to potentially harmful substances. Environmental factors such as EDCs, including per- and polyfluoroalkyl substances (PFASs) and cigarette smoking, have previously been shown to damage the post-pubertal ovarian tissue,[29,30] which in turn could affect the development of the oocyte pool of a daughter.[20,21,31] Both early and later ages at menarche have been reported in daughters who were exposed to PFAS in utero,[32] and maternal cigarette smoking in pregnancy has consistently been associated with earlier menarche in daughters.[14,33]

In terms of physiology, the childbirth-menopause interval is determined mainly by the number of oocytes a female has left in her ovaries at the time of childbirth and the rate of depletion of this ovarian reserve after childbirth, both of which show considerable inter-individual variation. We found that daughters born by mothers with >15 years left until menopause had a lower likelihood of experiencing early menarche. These mothers will, on average, have more oocytes left in their ovaries at the time of conception compared to those with a shorter time left until menopause.[34] In support of this, studies have found that women with diminished ovarian reserve

show signs of accelerated ovarian aging.[35] Accelerated ovarian aging has also been suggested in women who conceived by assisted reproductive technology,[36] a method of conception associated with earlier menarche in daughters.[25] It has further been hypothesized that offspring conceived from a near-depleted ovarian follicular reserve may have other reproductive characteristics compared to those conceived at an earlier stage of ovarian aging,[37] an idea also supported by data from animal studies.[38] This effect could be mediated by low-grade DNA damage in the oocyte, which occurs more frequently in oocytes ovulated closer to menopause,[39] or by the oocytes' mitochondrial content.[20,40]

After conception, the intrauterine milieu is another possible mechanism whereby maternal reproductive milestones could influence daughter's menarche. The size of the initial follicular pool in daughters is influenced by intrauterine conditions in some animals,[41] and there is speculation that the same could be the case in humans.[42] Also, there is evidence that some pregnancy complications that are more prevalent in mothers of advanced age, such as preterm birth[43] and hypertensive disorders in pregnancy[44] are associated with earlier puberty in the offspring. The use of ART is more prevalent among older mothers and is associated with both preterm birth and low birth weight, both of which are associated with early menarche in daughters.[25,45] Smoking is also associated with pregnancy complications,[46] as well as with early menopause in mothers.[47,48] On the other hand, younger mothers with premature ovarian insufficiency were not shown to have an increased risk of these pregnancy complications.[49]

Our stratified analysis showed results that were consistent with the main analyses for mothers with a normal age at menarche (12–14 years). As an additional finding, we confirmed a strong association between age at menarche in mothers and daughters, which is in line with several previous studies.[3,50] Based on data from The Danish National Birth Cohort, a study from 2019 on 7088 mother-daughter pairs reported a mean age at menarche of 13.0 years in Danish girls born between 2000 and 2003, 3.6 months earlier than their mothers.[50] Similarly, the Bergen Growth study found a mean age at menarche of 12.9 years for girls born between 2000 and 2009.[3]

Two Danish groups studied the association between parental age at childbirth and age at menarche in the offspring. Thomsen and co-workers[18] used data from The Danish National Birth Cohort and found no significant association between either of the parents' age at childbirth and age at menarche in daughters. Like Thomsen and co-workers, we found no association between age at childbirth in mothers and age at menarche in daughters in our partially adjusted analysis. In contrast, Shrestha and co-workers[17] included 3168 females born in 1984–1987 and found a 9-day earlier onset of menarche in daughters with each year increase in maternal age. However, estimates were not adjusted for maternal age at menarche in that study.

Strengths of our study include the large study sample, family data, longitudinal follow-up, and few missing data on relevant covariates. Age at menarche in mothers and daughters in the current study shows good agreement with previous studies on similar populations in Norway and Denmark.[1,3,50]

A potential limitation of our study is recall bias since both age at menarche and age at menopause were self-reported. However, recall time for age at menarche in daughters was short (mean 1.9 years) and reported at maximum of 22 years of age. Reproducibility of age at menarche has previously been shown to be high.[51] Age at menopause was reported with a mean recall time of 5.4 years, and a previous study showed that women experiencing early menopause (<45 years) overestimated their age at menopause, while women with late menopause (>55 years) tended to underestimate their age at menopause.[52] In our dataset, only 24 women reported an age at menopause >55 years, while 227 women reported an age at menopause <45 years.

Limiting our study is the need to include mothers who have reached menopause, which could cause selection bias by capturing a higher proportion of women with early menopause. This can be seen from Figure 2, where the distribution of age at menopause in our dataset has a left tail. The mean age at menopause in some recent studies is 5–52 years in Norway, and for the dataset used in our analysis, it was 48.4 years.[1] Also, the final study samples of 14 576 and 1350 participants are considerably lower than the original MoBa population. The necessity to include only complete mother-daughter pairs restricted the study sample substantially, which also could introduce bias. Further, we cannot rule out that misclassification bias has been introduced as information about hormone replacement therapy (HRT) was not available from the questionnaire that inquired about menopause. The use of HRT during perimenopause to combat hot flashes could, for instance, lead to cessation of menses as a side effect and, in this way, influence the mother's perceived timing of menopause. Since the use of HRT could either underestimate or overestimate the reported age at menopause, it could potentially bias associations in both directions.

MoBa mothers were recruited between 1999 and 2008, with maternal birth years ranging from 1956 to 1990. Due to the nature of the data collection, our dataset includes a higher proportion of older mothers from earlier birth cohorts and a higher proportion of younger mothers from more recent birth cohorts. Consequently, the age at childbirth in our dataset decreases over time, which does not reflect the trend in the general population. Further, between 1956 and 1990, several societal changes took place that contributed to the postponement of childbearing to more advanced ages. These changes include increased availability of hormonal contraceptives and education among women, as well as advancement in gender equality and a larger proportion of working women.[53] We aimed to account for some of these time trends when adjusting for maternal birth year in our models, and after doing so, we observed an increased effect of the menarche-childbirth interval on daughter's age at menarche. Interestingly we observed a similar trend when using the mothers age at childbirth as exposure. After additionally adjusting for mother's birth year, we found that being born to younger mothers (<29 years) gave a reduced likelihood of early menarche in the daughters, while being born to older mothers (>33 years) gave an increased likelihood of early menarche. We observed a similar pattern in our stratified analyses, where we

stratified the menarche-childbirth interval based on maternal age at menarche. However, this effect was not observed when using the interval between childbirth and menopause as exposure. These findings suggest that the odds of daughter's menarche vary across maternal birth cohorts, or that there may be unmeasured confounding factors influencing the result.

Finally, we lacked data on potentially harmful chemicals that might disturb reproductive milestones. Exposure to PFAS has, in some studies, been shown to be associated with age at menopause and age at menarche.[54,55]

5 | CONCLUSION

In this large population-based study, we found that being born <16 years after maternal menarche was associated with a lower likelihood of experiencing early menarche in daughters. In contrast, being born >20 years after maternal menarche was associated with a higher likelihood of experiencing early menarche compared to the reference category of daughters born 16–20 years after maternal menarche. These associations were strongly influenced by maternal birth year, and replication of these findings is warranted.

AUTHOR CONTRIBUTIONS

Mari Landås Warp and Hans Ivar Hanevik conceived the idea of the study; Siri E. Håberg obtained access to data. Mari Landås Warp and Hans Ivar Hanevik designed the study with important insight from Thea Grindstad, Karoline H. Skåra, Maria C. Magnus, Siri E. Håberg, Nils-Halvdan Morken, Cecilia H. Ramlau-Hansen, and Liv Bente Romundstad. Mari Landås Warp performed data analyses, interpreted the findings, and wrote the first version of the manuscript, supervised by Hans Ivar Hanevik. All authors contributed substantially to the interpretation of the data and to the critical revision of the manuscript.

FUNDING INFORMATION

This study was funded by the Norwegian Institute of Public Health, Oslo, Norway, by Telemark Hospital Trust, Porsgrunn, Norway, and was partly supported by the Research Council of Norway through its centers of excellence funding scheme, project number 262700 and project no. 320656. The project was Co-funded by the European Union (EU) (European Research Council, BIOSFER, 101071773). M.C.M. has received funding from the ERC under the EU's Horizon 2020 research and innovation program (INFERTILITY; grant agreement no. 947684).

CONFLICT OF INTEREST STATEMENT

The authors report no competing interests.

DATA AVAILABILITY STATEMENT

Data are available upon request by application to the Norwegian Mother, Father and Child Cohort study (mobaadm@fhi.no) and to www.helsedata.no. An ethical approval from The Regional Committee for Medical and Health Research Ethics in Norway is required for application.

ETHICS STATEMENT

The establishment of MoBa and initial data collection was based on a license from the Norwegian Data Protection Agency and approval from The Regional Committees for Medical and Health Research Ethics. Written consent was obtained from all participants at the time of recruitment. The MoBa cohort is currently regulated by the Norwegian Health Registry Act. Our study was approved by The Regional Committees for Medical and Health Research Ethics of South/East Norway on June 1, 2021 (project number 277291). The Medical Birth Registry of Norway is approved by the Norwegian Data Inspectorate. According to Norwegian regulations, the use of anonymous data does not require approval from an ethical board.

ORCID

Mari Landås Warp https://orcid.org/0009-0009-7613-6880

REFERENCES

1. Gottschalk MS, Eskild A, Hofvind S, Gran JM, Bjelland EK. Temporal trends in age at menarche and age at menopause: a population study of 312 656 women in Norway. *Hum Reprod*. 2020;35:464-471.
2. Dratva J, Gomez Real F, Schindler C, et al. Is age at menopause increasing across Europe? Results on age at menopause and determinants from two population-based studies. *Menopause*. 2009;16:385-394.
3. Bruserud IS, Roelants M, Oehme NHB, et al. References for ultrasound staging of breast maturation, tanner breast staging, pubic hair, and menarche in Norwegian girls. *J Clin Endocrinol Metab*. 2020;105:1599-1607.
4. Matthews TJ, Hamilton BE. First births to older women continue to rise. *NCHS Data Brief*. 2014;152:1-8.
5. Statistics Norway. 2024. https://www.ssb.no/en/statbank/table/05530/tableViewLayout1/
6. 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;39:812-821.
7. Zheng Y, Wen TS, Shen Y, Hu H. Age at menarche and cardiovascular health: results from the NHANES 1999–2016. *Menopause*. 2020;28:18-24.
8. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol*. 2012;13:1141-1151.
9. Brix N, Ernst A, Lauridsen LLB, et al. Maternal pre-pregnancy obesity and timing of puberty in sons and daughters: a population-based cohort study. *Int J Epidemiol*. 2019;48:1684-1694.
10. Morris DH, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ. Familial concordance for age at menarche: analyses from the breakthrough generations study. *Paediatr Perinat Epidemiol*. 2011;25:306-311.
11. Murabito JM, Yang Q, Fox C, Wilson PW, Cupples LA. Heritability of age at natural menopause in the Framingham heart study. *J Clin Endocrinol Metab*. 2005;90:3427-3430.
12. Day FR, Thompson DJ, Helgason H, et al. Genomic analyses identify hundreds of variants associated with age at menarche and support a role for puberty timing in cancer risk. *Nat Genet*. 2017;49:834-841.

13. Morris DH, Jones ME, Schoemaker MJ, Ashworth A, Swerdlow AJ. Familial concordance for age at natural menopause: results from the breakthrough generations study. *Menopause*. 2011;18:956-961.
14. Brix N, Ernst A, Lauridsen LLB, et al. Maternal smoking during pregnancy and timing of puberty in sons and daughters: a population-based cohort study. *Am J Epidemiol*. 2019;188:47-56.
15. Brix N, Ernst A, Lauridsen LLB, et al. Childhood overweight and obesity and timing of puberty in boys and girls: cohort and sibling-matched analyses. *Int J Epidemiol*. 2020;49:834-844.
16. Webster GD, Graber JA, Gesselman AN, Crosier BS, Schember TO. A life history theory of father absence and menarche: a meta-analysis. *Evol Psychol*. 2014;12:273-294.
17. Shrestha A, Nohr EA, Bech BH, Ramlau-Hansen CH, Olsen J. Parental age at childbirth and age of menarche in the offspring. *Hum Reprod*. 2010;25:799-804.
18. Thomsen AML, Ramlau-Hansen CH, Olsen J, et al. The influence of parental age on timing of puberty: a study in the Danish national birth cohort. *Scand J Public Health*. 2022;50:629-637.
19. Lopez-Rodriguez D, Franssen D, Bakker J, Lomniczi A, Parent AS. Cellular and molecular features of EDC exposure: consequences for the GnRH network. *Nat Rev Endocrinol*. 2021;17:83-96.
20. May-Panloup P, Boucret L, Chao de la Barca JM, et al. Ovarian ageing: the role of mitochondria in oocytes and follicles. *Hum Reprod Update*. 2016;22:725-743.
21. Avendano MS, Vazquez MJ, Tena-Sempere M. Disentangling puberty: novel neuroendocrine pathways and mechanisms for the control of mammalian puberty. *Hum Reprod Update*. 2017;23:737-763.
22. Alviggi C, Humaidan P, Howles CM, Tredway D, Hillier SG. Biological versus chronological ovarian age: implications for assisted reproductive technology. *Reprod Biol Endocrinol*. 2009;7:101.
23. te Velde ER, Pearson PL. The variability of female reproductive ageing. *Hum Reprod Update*. 2002;8:141-154.
24. Magnus P, Birke C, Vejrup K, et al. Cohort profile update: the Norwegian mother and child cohort study (MoBa). *Int J Epidemiol*. 2016;45:382-388.
25. Klemetti R, Perry B, Henningsen AKA, et al. Puberty disorders among ART-conceived singletons: a Nordic register study from the CoNARTaS group. *Hum Reprod*. 2022;37:2402-2411.
26. Telfer EE, Grosbois J, Odey YL, Rosario R, Anderson RA. Making a good egg: human oocyte health, aging, and in vitro development. *Physiol Rev*. 2023;103:2623-2677.
27. Hagen CP, Fischer MB, Wohlfahrt-Veje C, et al. AMH concentrations in infancy and mid-childhood predict ovarian activity in adolescence: a long-term longitudinal study of healthy girls. *EClinicalMedicine*. 2023;55:101742.
28. Aiken CE, Tarry-Adkins JL, Penfold NC, Dearden L, Ozanne SE. Decreased ovarian reserve, dysregulation of mitochondrial biogenesis, and increased lipid peroxidation in female mouse offspring exposed to an obesogenic maternal diet. *FASEB J*. 2016;30:1548-1556.
29. Ding N, Harlow SD, Randolph JF Jr, Loch-Caruso R, Park SK. Perfluoroalkyl and polyfluoroalkyl substances (PFAS) and their effects on the ovary. *Hum Reprod Update*. 2020;26:724-752.
30. Zenzes MT. Smoking and reproduction: gene damage to human gametes and embryos. *Hum Reprod Update*. 2000;6:122-131.
31. Lutterodt MC, Sorensen KP, Larsen KB, Skouby SO, Andersen CY, Byskov AG. The number of oogonia and somatic cells in the human female embryo and fetus in relation to whether or not exposed to maternal cigarette smoking. *Hum Reprod*. 2009;24:2558-2566.
32. Barrett ES, Rivera-Nunez Z. Invited perspective: PFAS and pubertal timing in girls—a maturing literature. *Environ Health Perspect*. 2023;131:91304.
33. Yermachenko A, Dvornyk V. A meta-analysis provides evidence that prenatal smoking exposure decreases age at menarche. *Reprod Toxicol*. 2015;58:222-228.
34. Kim C, Slaughter JC, Wang ET, et al. Anti-Mullerian hormone, follicle stimulating hormone, antral follicle count, and risk of menopause within 5 years. *Maturitas*. 2017;102:18-25.
35. de Boer EJ, den Tonkelaar I, te Velde ER, Burger CW, van Leeuwen FE, OMEGA-Project Group. Increased risk of early menopausal transition and natural menopause after poor response at first IVF treatment. *Hum Reprod*. 2003;18:1544-1552.
36. Lee Y, Bohlin J, Page CM, et al. Associations between epigenetic age acceleration and infertility. *Hum Reprod*. 2022;37:2063-2074.
37. Basso O, Willis SK, Hatch EE, Mikkelsen EM, Rothman KJ, Wise LA. Maternal age at birth and daughter's fecundability. *Hum Reprod*. 2021;36:1970-1980.
38. Zacchini F, Sampino S, Zietek M, Chan A. Delayed parenthood and its influence on offspring health: what have we learned from the mouse model. *Biol Reprod*. 2022;106:58-65.
39. Phillips KA, Collins IM, Milne RL, et al. Anti-Mullerian hormone serum concentrations of women with germline BRCA1 or BRCA2 mutations. *Hum Reprod*. 2016;31:1126-1132.
40. Kasapoglu I, Seli E. Mitochondrial dysfunction and ovarian aging. *Endocrinology*. 2020;161:bqaa001.
41. Evans AC, Mossa F, Walsh SW, et al. Effects of maternal environment during gestation on ovarian folliculogenesis and consequences for fertility in bovine offspring. *Reprod Domest Anim*. 2012;47(suppl. 4):31-37.
42. Depmann M, Faddy MJ, van der Schouw YT, et al. The relationship between variation in size of the primordial follicle pool and age at natural menopause. *J Clin Endocrinol Metab*. 2015;100:E845-E851.
43. Wehkalampi K, Hovi P, Dunkel L, et al. Advanced pubertal growth spurt in subjects born preterm: the Helsinki study of very low birth weight adults. *J Clin Endocrinol Metab*. 2011;96:525-533.
44. Lunddorf LLH, Brix N, Ernst A, et al. Hypertensive disorders in pregnancy and timing of pubertal development in daughters and sons. *Hum Reprod*. 2020;35:2124-2133.
45. Hvidt JJ, Brix N, Ernst A, Lauridsen LLB, Ramlau-Hansen CH. Size at birth, infant growth, and age at pubertal development in boys and girls. *Clin Epidemiol*. 2019;11:873-883.
46. Tarasi B, Cornuz J, Clair C, Baud D. Cigarette smoking during pregnancy and adverse perinatal outcomes: a cross-sectional study over 10 years. *BMC Public Health*. 2022;22:2403.
47. Mishra GD, Chung HF, Cano A, et al. EMAS position statement: predictors of premature and early natural menopause. *Maturitas*. 2019;123:82-88.
48. Shrestha A, Nohr EA, Bech BH, Ramlau-Hansen CH, Olsen J. Smoking and alcohol use during pregnancy and age of menarche in daughters. *Hum Reprod*. 2011;26:259-265.
49. Hu S, Xu B, Jin L. Perinatal outcome in young patients with diminished ovarian reserve undergoing assisted reproductive technology. *Fertil Steril*. 2020;114:118-124.e1.
50. Brix N, Ernst A, Lauridsen LLB, et al. Timing of puberty in boys and girls: a population-based study. *Paediatr Perinat Epidemiol*. 2019;33:70-78.
51. Lundblad MW, Jacobsen BK. The reproducibility of self-reported age at menarche: the Tromso study. *BMC Womens Health*. 2017;17:62.
52. Rodstrom K, Bengtsson C, Lissner L, Bjorkelund C. Reproducibility of self-reported menopause age at the 24-year follow-up of a population study of women in Goteborg, Sweden. *Menopause*. 2005;12:275-280.
53. Mills M, Rindfuss RR, McDonald P, te Velde E, Reproduction E, Society TF. Why do people postpone parenthood? Reasons and social policy incentives. *Hum Reprod Update*. 2011;17:848-860.
54. Ernst A, Brix N, Lauridsen LLB, et al. Exposure to perfluoroalkyl substances during fetal life and pubertal development in boys and girls from the Danish national birth cohort. *Environ Health Perspect*. 2019;127:17004.

55. Ding N, Harlow SD, Randolph JF, et al. Associations of perfluoroalkyl substances with incident natural menopause: the study of women's health across the nation. *J Clin Endocrinol Metab*. 2020;105:e3169-e3182.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Warp ML, Grindstad T, Skåra KH, et al. Maternal time interval between menarche and childbirth is associated with daughter's age at menarche. *Acta Obstet Gynecol Scand*. 2025;104:1101-1111. doi:10.1111/aogs.15088