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Childhood experiences of parenting and age at menarche, age at menopause and duration of reproductive lifespan: Evidence from the English Longitudinal Study of Ageing

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ABSTRACT

Objectives: The parent-child relationship is critical for human development, yet little is known about its association with offsprings' reproductive health outside the context of abuse and neglect. We investigated whether childhood experiences of poor-quality parenting (characterized as decreased parental care and increased parental overprotection) are associated with women's reproductive timing and lifespan.
Study design: Observational study of 2383 women aged 55–89 years in 2007 from the English Longitudinal Study of Ageing (ELSA). Multinomial logistic regression models were estimated.
Main outcome measures: Self-reported ages at menarche and menopause and duration of reproductive lifespan.
Results: Increasing maternal and paternal overprotection were associated with later menarche (≥16 years) after adjustment for age and childhood socioeconomic position (relative risk ratio (RRR) 1.11, 95% CI 1.02–1.21 and 1.11, 95% CI 1.01–1.21, respectively, per unit increase in the predictor). Increasing parental overprotection and decreasing paternal care were associated with earlier menarche (≤10 years). However, these associations were marginally non-significant. Maternal and paternal overprotection were also inversely associated with age at natural menopause after adjustment for age, childhood socioeconomic position and age at menarche (p value for linear trend = 0.041 and 0.004, respectively). Further, increasing paternal overprotection was associated with a shorter reproductive lifespan (≤33 years) (RRR 1.09 (1.01–1.18), per unit increase in the predictor) after adjustment for age and childhood socioeconomic position. Adjustment for additional childhood and adult factors did not explain these associations.
Conclusions: Women who experienced poor-quality parenting in childhood, especially increased levels of parental overprotection, might be at increased risk of an unfavourable reproductive health profile that is characterized by late or early menarche, premature menopause and a shorter reproductive lifespan.

1. Introduction

Menarche and menopause are two landmarks in women's reproductive history that define the duration of reproductive lifespan. They are also major determinants of women's health. Early menarche is associated with a number of health problems, including an unfavourable cardiovascular risk profile, and increased risk of breast, endometrial and ovarian cancer, and mortality [1–5]. Late menarche has been associated with health symptoms and conditions such as asthma [2]. Premature and early menopause are associated with an increased risk of chronic conditions including cardiovascular disease and mortality [6,7], while late menopause has been linked to an increased risk of breast, endometrial and ovarian cancer [1,5,8]. The duration of reproductive lifespan has also been associated with health problems, such as cardiovascular disease [9] and hormone-sensitive cancers, such as breast cancer [1].

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Evidence suggests that childhood family environment can affect the timing of both menarche and menopause [10]. There is an extensive literature on the importance of abuse, neglect and an unfavourable family environment in the determination of age at menarche (AAM) [11–13], while familial and parental factors are also associated with earlier menopause [10]. However, most of this evidence stems from studies of smaller selective samples with only few studies having used large or nationally representative samples to examine the associations between the childhood experiences of parenting and AAM [14–16], age at natural menopause (AANM) and duration of reproductive lifespan in the offspring [14]. For this reason, and because the parent-child relationship is critical for human development and childhood experiences of poor quality parenting are associated with increased risk of mortality [17] and cancer [18], we studied whether childhood experiences of poor quality parenting were also associated with AAM, AANM and the duration of reproductive lifespan in a national sample of older women. Drawing on earlier research [19], we defined poor quality parenting as low levels of paternal and maternal care and affection and high levels of paternal and maternal overprotection. Our hypothesis is that poor quality parenting is a potent childhood stressor and as such it could influence women's reproductive timing and health over the life course in multiple ways.

2. Methods

2.1. Study population

Our sample was drawn from the English Longitudinal Study of Aging (ELSA) (www.elsa-project.ac.uk). ELSA is an ongoing nationally representative observational study that begun in 2002-03 (ELSA wave 1) with a sample of 11,391 individuals (6205 women) aged ≥50 years. For the needs of our study, we used data from the second follow-up interview (ELSA wave 3), which took place in 2006-07, and the 2007 ELSA Life History Interview, which was an one-off survey that collected retrospective information about the material circumstances, experiences and health of the ELSA participants before joining ELSA.

4181 women participated in ELSA wave 3 of whom 3442 participated in the ELSA Life History Interview. The analytical sample comprised 2383 women aged ≥55 years in 2007 after the exclusion of 59 women due to very old age (≥90 years), 491 women who did not complete the childhood experiences questionnaire, 298 women with missing values in the parenting measures, 180 women who were not reared by both natural parents and 31 with missing information on AAM (including 2 with AAM > 20 years). For the needs of the AANM and duration of reproductive lifespan analyses, we used an analytical sample of 1674 women, after further excluding 561 women who experienced non-natural menopause (including 11 with missing information on age at menopause), 84 who had their natural menopause at unusually old > 60 or young age < 30 years, and 64 with missing values in covariates. The sample selection flowchart can be found in the Online Supplement (eFigure 1).

ELSA has been approved by the London Multi-Centre Research Ethics Committee (MREC/01/2/91) and informed consent has been obtained by the participants.

2.2. Measures of childhood experiences of parenting

Parenting was measured as part of the ELSA Life History interview using the seven-item Parental Bonding Instrument (PBI). PBI is designed to collect retrospective information about the childhood experiences of parenting (at age ≤15 years) in adult samples and focuses on two fundamental dimensions of parenting, care and overprotection. Parental care refers to parental emotional warmth, affection, empathy, closeness and care for one's child as opposed to emotional coldness, indifference and neglect [19]. Parental overprotection refers to parental control, overprotection, intrusion, excessive contact and prevention of independent behaviour as opposed to allowance of independence and autonomy [19]. The seven-item PBI includes three care and four overprotection items and can be found here: https://bit.ly/2LqwFMx (see question 1). We generated care and overprotection summary scores for both natural parents. To avoid the unnecessary exclusion of participants with few missing values in any of the parenting scales, we imputed up to one missing value per scale with the mean score of that scale (maternal overprotection was the scale with the largest number of such imputations, n = 69). For comparison reasons, the analyses of the non-imputed data are presented in eTables 1–3.

2.3. Reproductive health outcomes

Information on women's health and reproductive history was self-reported and retrospectively collected. AAM, the age at first menstrual period, was measured as an ordinal variable with the following categories: ≤10, 11, 12, 13, 14, 15 and ≥16 years. AANM, was calculated by subtracting the year of birth from the year of last menstrual period for women who had natural menopause. We categorized the continuous AANM variable as follows: 30–39 years (premature menopause), 40–44 years (early menopause), 45–52 years and 53–60 years (late menopause). The duration of reproductive lifespan was calculated by subtracting AAM from AANM and categorized into groups of 3-year incremental differences [9] as follows: ≤33 years, 34–36 years, 37–39 years, ≥40 years.

2.4. Statistical analyses

We estimated multinomial logistic regression models. The predictor measures were used as continuous variables. For clarity purposes, maternal and paternal care scores were reversed, with higher scores indicating decreased care. The risk estimates denote change in the outcome measure per unit decrease in maternal and paternal care scores or per unit increase in maternal and paternal overprotection scores. When modelling AAM, first, we estimated the unadjusted associations, which we then adjusted for age and childhood socioeconomic position (father's or main carer's occupation when respondent aged 14 years and number of books in the household when respondent aged 10 years). We followed a different modelling approach when analysing AANM and duration of the reproductive lifespan. We first estimated the unadjusted associations, which we then initially adjusted for age, and childhood socioeconomic position (in the AANM analyses we also included AAM in this model), and then adult socioeconomic position (education and total net non-pension household wealth including property, savings, and other assets), marital status, adult obesity (body mass index and waist circumference), lifetime smoking, and parity. In supplementary analyses, we adjusted our models for a number of additional childhood and adult factors that could have confounded the associations (see eTables 1–3).

3. Results

The mean age of the sample was 67.9 years (Table 1). The mean AANM was 50.3 years, the mean AAM was 13 years, and mean duration of reproductive lifespan was 37.2 years (Table 1). Childhood experiences of poor parenting were related with AAM (Table 2). Increasing paternal and maternal overprotection were significantly associated with a later menarche (≥16 years) (age- and childhood SEP-adjusted relative risk ratio (RRR): 1.11, 95% CI, 1.01, 1.21 and 1.11, 95% CI, 1.02, 1.21, respectively, per unit increase in the predictor). Along with decreasing paternal care, they were also associated with early menarche (≤10 years), but these associations were marginally non-significant. Further, we observed inverse associations between paternal and maternal overprotection and AANM (*P value* for linear trend: 0.004 and 0.041, respectively, after adjustment for age, childhood socioeconomic position and AAM) (Table 3). Finally, we found that paternal

Table 1
The baseline characteristics of the sample, English Longitudinal Study of Ageing, 2007 (n = 2383).[a]

	N[a] (%)
Mean age (SD)	67.9 (8.8)
Paternal or main carer's occupation when respondent aged 14 years	
Manager/professional/administrator/own business	837 (35.1)
Trade/care/sales/services	724 (30.4)
Manual or casual jobs/unemployed	722 (30.3)
Other (including retired)	100 (4.2)
Number of books in the household when respondent aged 10 years	
Enough to fill two bookcases or more (> 100 books)	474 (19.9)
Enough to fill one bookcase (26 to 100 books)	705 (29.6)
Enough to fill one shelf (11 to 25 books)	585 (24.5)
None or very few (0 to 10 books)	531 (22.3)
Missing	88 (3.7)
Current marital status	
Married	1514 (63.5)
Non-married	869 (36.5)
Education	
A-level or higher	765 (32.1)
Secondary or equivalent	830 (34.8)
No educational qualifications	788 (33.1)
Total household wealth (N = 2335)	
Wealthiest tertile (≥£304,000)	787 (33.7)
Intermediate tertile (< £304,000 & ≥£157,500)	782 (33.5)
Lowest tertile (< £157,500)	766 (32.8)
Smoking	
Never	1098 (46.1)
Ex-smoker	1005 (42.2)
Current smoker	280 (11.7)
Body mass index (kg/m^2) (categories)	
< 25	635 (26.7)
≥25 to < 30	794 (33.3)
≥30	637 (26.7)
Missing	317 (13.3)
Waist circumference (categories)	
< 94 cm in men / < 80 cm in women	435 (18.3)
94 to 101 cm in men / 80 to 87 cm in women	490 (20.6)
≥102 cm in men / 88 cm in women	1183 (49.6)
Missing	275 (11.5)
N of natural children (parity)	
None	336 (14.1)
1 child	441 (18.5)
2 children	935 (39.2)
≥3 children	671 (28.2)
Mean age at natural menopause (SD) (n = 1674)	50.3 (4.6)
Age at natural menopause (categories) (n = 1674)	
< 40 years (premature menopause)	34 (2.1)
40 to 44 years (early menopause)	136 (8.1)
45 to 52 years	958 (57.2)
≥53 years (late menopause)	546 (32.6)
Mean age at menarche (SD)	13.0 (1.7)
Age at menarche (categories)	
≤10 years	120 (5.0)
11 years	394 (16.5)
12 years	366 (15.4)
13 years	543 (22.8)
14 years	504 (21.2)
15 years	291 (12.2)
≥16 years	165 (6.9)
Mean duration of reproductive lifespan (SD) (n = 1674)	37.2 (4.9)
Duration of reproductive lifespan (categories) (n = 1674)	
≤33 years	309 (18.5)
34 to 36 years	334 (19.9)
37 to 39 years	480 (28.7)
≥40 years	551 (32.9)

[a] Unless otherwise stated.

overprotection was associated with a shorter reproductive lifespan (≤33 years) (RRR: 1.09, 95% CI, 1.01, 1.18, per unit increase in the predictor, after adjustment for age, childhood socioeconomic position and AAM) (Table 4). Additional adjustments for childhood and adult covariates did not explain these associations.

4. Discussion

In a national sample of older women, we found childhood experiences of poor parenting to be associated with an unfavourable reproductive health profile characterized by late or early menarche, premature natural menopause and a shorter reproductive lifespan. Maternal care, which is the most extensively studied parental factor in both animals and humans, appears to be less important for women's reproductive timing than parental overprotection, which was associated with both age at menarche and age at natural menopause. The preponderance of parental overprotection as a childhood determinant of reproductive development and lifespan over parental care is not surprising and concurs with literature highlighting parental overprotection as a risk factor for psychosocial development [20], and meta-analytic evidence suggesting that autonomy restriction, which is a hallmark of overprotective parenting, is the parental factor most strongly associated with an increased risk of depression in adolescence [21].

Our findings highlight the importance of the role of father for daughters' reproductive lifespan. Paternal overprotection was more strongly associated with a shorter reproductive lifespan than maternal overprotection in our data. There is extensive literature on the role of the father in the determination of AAM in the female offspring [12,13,22,24]. From an evolutionary perspective, fathers, unlike mothers, are expected to grant more autonomy, encourage independence, and prepare the offspring for the challenges of the life outside the family environment [23]. Based on this evidence, we can speculate that having an autonomy-restricting overprotective father can be more stressful and because of that potentially more harmful and more strongly associated with a shorter female offspring reproductive lifespan than having an overprotective mother.

4.1. Previous evidence

Our findings are partially discordant with those of a recent study that did not find an association between maternal overprotection and AAM [14]. Evidence suggests that a stressful family environment that is characterized by family conflict and disruption and father's absence is associated with earlier menarche [12]. Studies that specifically examined factors such as a parental control over the child reported that harsh maternal and paternal control were associated with younger age at menarche [11]. Our findings partially concur with this evidence. We found associations between decreased parental care and increased parental overprotection and both early menarche (≤10 years) (these associations were borderline non-significant though) and late menarche (≥16 years). Our findings are also concordant with evidence from national birth cohort studies suggesting that parental abuse is strongly associated with late menarche and more weakly with early menarche [16], and that parental neglect, that is lack of interest in the offspring at age 7 years, is strongly associated with later menarche [15].

Fewer studies have examined the association between familial factors in childhood and menopause. Our findings are consistent with evidence suggesting an association between an unfavourable family environment in childhood that is characterized by conflict and parental divorce and an earlier age at menopause [25], but are at odds with findings suggesting that maternal overprotection is not associated with AANM and reproductive lifespan [14].

4.2. Strengths and weaknesses

Evidence on the association between childhood experiences of parenting and women's reproductive lifespan from large well-characterized studies is scarce. Our findings substantially add to the literature and improve our understanding of this relationship. The use of data from a nationally representative study such as ELSA also makes our findings more generalizable to community-dwelling women aged ≥55 years. Further, in complementary analyses, we were able to

Table 2
The associations between parenting measures and age at menarche[a] (N = 2383).

	≤10 years (n = 120)	11 years (n = 394)	12 years (n = 366)	13 years (reference category) (n = 543)	14 years (n = 504)	15 years (n = 291)	≥16 years (n = 165)
Maternal Care Score (range: 0-highest levels of care to 9-lowest levels of care)							
Model 1[b]	1.04 (0.94 to 1.14)	1.02 (0.96 to 1.09)	1.02 (0.95 to 1.09)	1.00	1.01 (0.95 to 1.08)	0.99 (0.92 to 1.07)	1.04 (0.95 to 1.13)
Model 2[c]	1.03 (0.94 to 1.14)	1.02 (0.95 to 1.09)	1.02 (0.95 to 1.09)	1.00	1.02 (0.95 to 1.08)	1.00 (0.93 to 1.08)	1.04 (0.95 to 1.14)
Maternal Overprotection Score (range: 0-lowest levels of overprotection to 12-highest levels of overprotection)							
Model 1[b]	1.08 (0.98 to 1.18)	1.05 (0.99 to 1.12)	1.02 (0.96 to 1. 09)	1.00	1.04 (0.98 to 1.10)	1.00 (0.93 to 1.07)	1.11 (1.02 to 1.21)[d]
Model 2[c]	1.08 (0.98 to 1.18)	1.05 (0.99 to 1.12)	1.02 (0.96 to 1.09)	1.00	1.04 (0.98 to 1.11)	1.00 (0.93 to 1.07)	1.11 (1.02 to 1.21)[d]
Paternal Care Score (range: 0- highest levels of care to 9-lowest levels of care)							
Model 1[b]	1.09 (0.99 to 1.21)	1.03 (0.96 to 1.11)	1.00 (0.93 to 1.07)	1.00	0.99 (0.93 to 1.06)	0.97 (0.90 to 1.05)	1.03 (0.94 to 1.14)
Model 2[c]	1.09 (0.99 to 1.21)	1.02 (0.95 to 1.10)	0.99 (0.92 to 1.07)	1.00	1.00 (0.93 to 1.07)	0.98 (0.90 to 1.06)	1.04 (0.95 to 1.15)
Paternal Overprotection Score (range: 0-lowest levels of overprotection to 12-highest levels of overprotection)							
Model 1[b]	1.07 (0.97 to 1.18)	1.04 (0.97 to 1.11)	0.99 (0.93 to 1.06)	1.00	1.02 (0.96 to 1.08)	1.01 (0.94 to 1.09)	1.10 (1.00 to 1.20)[d]
Model 2[c]	1.07 (0.97 to 1.18)	1.03 (0.97 to 1.11)	0.99 (0.92 to 1.06)	1.00	1.02 (0.96 to 1.09)	1.01 (0.94 to 1.09)	1.11 (1.01 to 1.21)[d]

[a] The estimates are relative risk ratios and denote change in the risk of experiencing younger or older age at menarche compared with the reference category per unit change in the predictor variable.
[b] This is the unadjusted association.
[c] Model 2 is adjusted for age and childhood socioeconomic position (i.e. number of books in the household at age 10 years, and father's or main carer's occupational class at age 14 years).
[d] $P \leq 0.05$.

ascertain that adjustment for known childhood risk factors, such as childhood experiences of abuse and parental mental health and addiction problems, and adult risk factors, such as history of cancer, did not explain the observed associations. Finally, the use of PBI, which is a validated widely used instrument of parenting experiences, makes the replication of our work by future research easier.

Our study has weaknesses that should be considered. Its observational design makes it impossible to account for all potential confounders and eliminate the possibility of spurious associations. Further, our study adopted a simple "traditional" mediation approach, which allows neither a fuller exploration of the interrelationships between the study variables nor the estimation of direct and indirect effects. However, the diversity of our findings, that is different parenting measures being associated with three different outcome measures, and their consistency with earlier findings [17,18], makes it unlikely that they are a statistical artefact caused by unaccounted confounding. Further, in complementary analyses, we also found that potentially confounding factors that might introduce recall bias, such as mood and memory impairment, did not alter our findings.

The use of retrospectively collected childhood data makes our findings susceptible to measurement bias. Nevertheless, our parenting and childhood socioeconomic position measures have been used before and found to have good predictive validity, while a comparison of our retrospective menarche and menopause data with those of previous reports [26] provides good evidence for their validity, including capturing the well-documented downward secular trend in age at menarche (eTable 4 and eFigure 2). The same applies to reproductive lifespan duration; our estimate of mean lifespan duration of 37.2 years is almost identical with estimates reported by large US studies [9,27]. Further, the concordance of our findings with those from national birth cohort studies is reassuring and likely indicates that the observed associations represent real phenomena.

Table 3
The association between parenting measures and age at natural menopause[a] (N = 1674).

	30 to 39 years (premature menopause) (n = 34)	40 to 44 years (early menopause) (n = 136)	45 to 52 years (reference category) (n = 958)	53 to 60 years (n = 546)	*P* value for linear trend
Maternal Care Score					
Model 1[b]	1.08 (0.92 to 1.28)	0.97 (0.88 to 1.07)	1.00	1.00 (0.94 to 1.05)	0.74
Model 2[c]	1.15 (0.96 to 1.37)	0.96 (0.87 to 1.06)	1.00	0.99 (0.93 to 1.05)	0.55
Model 3[d]	1.15 (0.96 to 1.37)	0.96 (0.87 to 1.06)	1.00	0.99 (0.93 to 1.05)	0.54
Maternal Overprotection Score					
Model 1[b]	1.09 (0.92 to 1.28)	0.97 (0.89 to 1.07)	1.00	0.94 (0.89 to 0.99)[e]	0.040
Model 2[c]	1.12 (0.94 to 1.34)	0.97 (0.88 to 1.06)	1.00	0.94 (0.89 to 0.99)[e]	0.041
Model 3[d]	1.13 (0.93 to 1.36)	0.96 (0.87 to 1.05)	1.00	0.94 (0.89 to 0.99)[e]	0.035
Paternal Care Score					
Model 1[b]	1.08 (0.91 to 1.30)	1.03 (0.93 to 1.14)	1.00	1.01 (0.95 to 1.07)	0.57
Model 2[c]	1.14 (0.95 to 1.38)	1.03 (0.93 to 1.14)	1.00	1.00 (0.94 to 1.06)	0.40
Model 3[d]	1.13 (0.93 to 1.37)	1.04 (0.94 to 1.15)	1.00	1.00 (0.94 to 1.07)	0.35
Paternal Overprotection Score					
Model 1[b]	1.14 (0.97 to 1.34)	1.02 (0.93 to 1.11)	1.00	0.94 (0.89 to 1.00)[e]	0.007
Model 2[c]	1.20 (1.01 to 1.43)[e]	1.01 (0.92 to 1.11)	1.00	0.94 (0.89 to 0.99)[e]	0.004
Model 3[d]	1.18 (0.98 to 1.40)	1.01 (0.92 to 1.11)	1.00	0.94 (0.89 to 0.99)[e]	0.005

[a] The estimates are relative risk ratios and denote change in the risk of experiencing premature, early or later menopause compared with the reference category per unit change in the predictor variable.
[b] This is the unadjusted association.
[c] Model 2 is adjusted for age, childhood socioeconomic position (i.e. number of books in the household at age 10 years and father's or main carer's occupational class at age 14 years), and age at menarche.
[d] Model 3 is adjusted for age, childhood socioeconomic position (i.e. number of books in the household at age 10 years and father's or main carer's occupational class at age 14 years), age at menarche, adult socioeconomic position (i.e. education and total net household wealth), marital status, smoking, body mass index, waist circumference, and parity.
[e] $P \leq 0.05$.

Table 4
The association between parenting measures and duration of the reproductive lifespan[a] (N = 1674).

	≤33 years (n = 309)	34 to 36 years (n = 334)	37 to 39 years (reference category) (n = 480)	≥40 years (n = 551)
Maternal Care Score				
Model 1[b]	0.99 (0.92 to 1.06)	0.99 (0.92 to 1.07)	1.00	1.00 (0.93 to 1.06)
Model 2[c]	1.00 (0.92 to 1.08)	1.00 (0.93 to 1.08)	1.00	1.00 (0.93 to 1.06)
Model 3[d]	0.99 (0.92 to 1.07)	1.00 (0.93 to 1.08)	1.00	1.00 (0.93 to 1.06)
Maternal Overprotection Score				
Model 1[b]	1.03 (0.96 to 1.11)	1.07 (1.00 to 1.15)[e]	1.00	1.00 (0.94 to 1.06)
Model 2[c]	1.03 (0.96 to 1.11)	1.08 (1.00 to 1.16)[e]	1.00	1.00 (0.94 to 1.07)
Model 3[d]	1.03 (0.96 to 1.11)	1.08 (1.00 to 1.16)[e]	1.00	1.00 (0.94 to 1.07)
Paternal Care Score				
Model 1[b]	1.03 (0.95 to 1.12)	0.99 (0.92 to 1.07)	1.00	1.03 (0.96 to 1.10)
Model 2[c]	1.05 (0.97 to 1.14)	1.00 (0.92 to 1.08)	1.00	1.03 (0.96 to 1.10)
Model 3[d]	1.06 (0.97 to 1.15)	1.00 (0.92 to 1.08)	1.00	1.03 (0.96 to 1.11)
Paternal Overprotection Score				
Model 1[b]	1.08 (1.01 to 1.17)[e]	1.09 (1.01 to 1.17)[e]	1.00	1.02 (0.96 to 1.09)
Model 2[c]	1.09 (1.01 to 1.18)[e]	1.10 (1.02 to 1.18)[e]	1.00	1.02 (0.96 to 1.09)
Model 3[d]	1.10 (1.02 to 1.19)[e]	1.10 (1.02 to 1.19)[e]	1.00	1.03 (0.97 to 1.10)

[a] The estimates are relative risk ratios and denote change in the risk of having a shorter or longer reproductive lifespan compared with the reference category per unit change in the predictor variable.
[b] This is the unadjusted association.
[c] Model 2 is adjusted for age and childhood socioeconomic position (i.e. number of books in the household at age 10 years and father's or main carer's occupational class at age 14 years).
[d] Model 3 is adjusted for age, childhood (i.e. number of books in the household at age 10 years and father's or main carer's occupational class at age 14 years), and adult socioeconomic position (i.e. education and total net household wealth), marital status, smoking, body mass index, waist circumference, and parity.
[e] $P \leq 0.05$.

Non-response is another source of bias in our data. The overall individual response rate in ELSA wave 3 (after excluding people who died, became institutionalized or migrated) was 73%, with no noticeable gender differences. 84.4% of responders in wave 3 participated in the ELSA Life History in 2007 [28], but again not of all of these people completed the self-completion questionnaire on childhood experiences that contained the parenting questions. Analyses of non-response in the ELSA Life History survey found significant differences in key characteristics such as socioeconomic position and health between responders and non-responders [17,29]. Based on these earlier findings, we can speculate that to an extent our findings are likely biased towards the null. Finally, statistical power is an issue as some analytical categories contained a relatively small number of participants and this led to wider 95% CI and increased uncertainty.

4.3. Pathways – poor quality parenting and age at menarche

Childhood experiences of poor parenting appear to be associated with AAM independently of low childhood socioeconomic position, adverse childhood experiences, such as abuse and parental mental health and addiction problems, and childhood health problems known to affect parenting. Notwithstanding our inability to account for other risk factors, such as maternal AAM, and childhood nutrition and obesity, these key findings point to the direction of a direct biological effect that can at least partially explain the association. Poor quality parenting can be a chronic childhood stressor that may induce chronic alterations and dysregulations in the function of the neuroendocrine and immune systems and affect the developing brain, which in turn, could affect AAM.

We found that childhood experiences of poor parenting were associated with late menarche. We also found marginally non-significant associations between childhood experiences of poor parenting and early menarche. Considered together, these findings indicate that the effect of stress stemming from poor parenting experiences in childhood on AAM is not unidirectional and possibly there are important modifiers that determine the direction of this association. A recent review suggested that one such modifier might be the timing of the action of stressors, with early life stress leading to an earlier onset of puberty and juvenile or peripubertal stress delaying the onset of puberty [30]. Another such modifier can be genes. Evidence supports a gene-environment interaction hypothesis as the quality of the family environment has been found to be positively associated with AAM in participants homozygous for minor alleles of the estrogen receptor alpha gene (*ESR1)*, but not in participants with other *ESR1* genotypes [31].

For any childhood exposure to delay or accelerate puberty and menarche, it should ultimately influence the activation of the hypothalamic–pituitary–gonadal (HPG) axis, whose core component is the pulsatile secretion of the Gonadotropin-releasing Hormone (GnRH) by hypothalamic GnRH neurons. GnRH is necessary for the secretion of gonadotropins, that is the follicle-stimulating hormone (FSH) and luteinizing hormone (LH), which are master regulators of the menstrual cycle and necessary for ovulation. Stress stemming from poor parenting experiences in childhood could affect multiple pathways involved in the activation of GnRH pulse generator. It may inhibit kisspeptin-mediated GnRH release. Kisspeptin (Kiss1) is a protein that plays a key stimulatory role in the activation of the GnRH pulse generator and the initiation of menarche [32]. It may also delay the onset of puberty via gamma-amino butyric acid- (GABA) and glutamate-mediated pathways [30], which play a critical role in the pubertal release of GnRH [33]. Further, chronic stress in childhood stemming from experiences of poor quality parenting may also affect AAM by inducing epigenetic alterations [34].

4.4. Pathways – poor quality parenting and age at natural menopause

Low socioeconomic position, lifetime smoking, obesity, history of cancer, ages at menarche and first natural birth, and parity did not explain the association between poor quality parenting and AANM. Based on these findings, we hypothesize that childhood experiences of poor quality parenting could be directly associated with a younger AANM via biological mediating pathways. Multiple stress-related pathways might be implicated in this association, however all these pathways should influence a single biological parameter of crucial importance, the ovarian reserve, the number of non-growing primordial follicles in the ovaries.

A dysregulated stress system and prolonged activation of the HPA

axis are expected to suppress the function of the HPG axis and the secretion of FSH and LH [35] and increase follicular atresia and degeneration [36]. Chronic stress could also affect the function of sympathetic nervous system, which releases norepinephrine in peripheral tissues. In the ovaries, norepinephrine is critical in the regulation of follicular development, ovulation and ovarian steroidogenesis [37]. Of importance in explaining our findings might also be stress-related pathways implicated in the decrease of the ovarian reserve before puberty, when the HPG axis is inactive. Such pathways may involve growth factors such as members of the transforming growth factor-β (TGF-β) superfamily [38], whose overactivation due to suppression of their regulators resulted in a considerable decrease of the ovarian reserve in prepubertal mice [39]. Also very important for premature menopause and regulated by growth factors, such as the insulin-like growth factor 1 (IGF1), is the intracellular phosphatidylinositol 3-kinase/Akt/mammalian target of rapamycin (PI3K/Akt/mTOR) signaling pathway, which is the master regulator of follicular activation and proliferation [40]. Increased activity of PI3K and mTOR may lead to increased activation of primordial follicles and premature "exhaustion" of the ovarian reserve. PI3K and mTOR pathways are also downregulated by different factors including oxytocin, a hypothalamic hormone that is related to maternal bonding with the newborn baby and parental behaviour, and its levels are lower in people who have experienced childhood adversity [41].

4.5. Conclusions

Using retrospectively collected childhood data, we found that childhood experiences of parenting might be a lifelong determinant of women's reproductive timing and lifespan independently of other childhood and adult risk factors. On the understanding that these findings cannot simply be an artefact of measurement error and selection bias, our study adds to the current understanding of the role of childhood factors in women's reproductive health. The importance of AAM and AANM for many health conditions, including cardiovascular disease, cancer and mortality, and the relevance of parenting to the vast majority of the population add to the scientific and societal value of our findings. Based on the assumption that poor quality parenting is a modifiable trait, our findings can inform prevention strategies and health policies. Future research should try to replicate our findings and add to the exploration of the association between childhood experiences of poor quality parenting and reproductive lifespan in women.

Contributors

Panayotes Demakakos conceived and designed the study, analyzed data and drafted the manuscript.

Nora Pashayan, Georgios Chrousos, Eleni Linara-Demakakou and Gita D. Mishra contributed to the design of the study, and critically revised the manuscript for important intellectual content and approved its submission.

Conflict of interest

The authors declare that they have no conflict of interest.

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Ethical approval

This study has been conducted in accordance with all relevant ethical regulations. It involves the analysis of publicly available secondary data from the ELSA study (www.elsa-project.ac.uk). ELSA has been approved by the London Multi-Centre Research Ethics Committee (MREC/01/2/91) and informed consent has been obtained by all ELSA participants.

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

The ELSA data can be downloaded from the UK Data Service: https://beta.ukdataservice.ac.uk/datacatalogue/studies/study?id=5050.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.maturitas.2019.01.010.

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