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Adverse childhood experiences and age at menopause: a bi-national cross-sectional analysis of the UK Biobank and US Health and Retirement Study

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Abstract

Background

Adverse childhood experiences (ACE) represent a pervasive global health burden, yet evidence regarding their association with age at menopause remains inconsistent and largely derived from single-cohort studies. This cross-national study aimed to investigate the association between ACE and age at menopause across two large-scale cohorts.

Methods

This cross-sectional analysis included 34,872 women from the UK Biobank and 5,163 from the Health and Retirement Study. Cumulative ACE scores were derived using validated instruments. Multivariable linear and logistic regression models assessed the associations of ACE with age at menopause (continuous) and early menopause (< 40, < 45, and < 48 years). Subgroup analyses examined effect modification across socioeconomic and behavioral strata.

Results

Higher ACE scores were significantly associated with earlier menopause in both cohorts (UKB: β = -0.074, 95% CI: -0.116 to -0.032; HRS: β = -0.254, 95% CI: -0.372 to -0.136) and with increased odds of early menopause, demonstrating a significant dose-response relationship. Direct maltreatment drove the association in UKB, whereas parental death was the predominant driver in HRS. The associations remained consistent across most subgroups, with area-level deprivation potentially intensifying the effects.

Conclusion

ACE is consistently associated with earlier menopause across two national cohorts. These findings underscore the enduring reproductive consequences of childhood adversity and suggest that routine ACE screening—particularly in socioeconomically deprived areas—may help identify women at heightened risk for accelerated reproductive aging and facilitate targeted preventive interventions.

1. Introduction

Women's health is a major public health concern, and menopause represents a critical transitional phase in the female lifespan with significant biological and clinical implications[1]. As a natural physiological process, menopause not only marks the cessation of menstrual cycles and the loss of fertility but is also widely recognized as an important indicator of overall health status and aging in women[2]. The timing of menopause varies considerably across individuals, and this variation has profound health consequences. Early menopause has been significantly linked to elevated risks of cardiovascular disease, osteoporosis, diabetes, cognitive decline, and all-cause mortality. In contrast, late menopause is associated with increased risks of breast and endometrial cancers[3–8]. Given these substantial health implications, understanding the factors that influence age at menopause holds important value for exploring healthy aging, disease risk, and the development of targeted prevention strategies.

Adverse childhood experiences (ACE)—encompassing various forms of abuse, neglect, and household dysfunction—represent a substantial public health burden worldwide. A recent large-scale meta-analysis synthesizing data from 1,002 studies across 102 countries estimated that approximately 28% of adults globally have experienced emotional abuse, 22% emotional neglect, 18% physical abuse, and 11% sexual abuse during childhood, with household dysfunction such as parental divorce or separation (24%) and household substance abuse (22%) being equally prevalent[9]. These alarming figures underscore that childhood adversity is not a rare phenomenon but rather a pervasive global issue with profound implications for lifelong health.

A growing body of evidence has documented the enduring impact of early-life factors on health outcomes across the life course [10]. Beyond the immediate psychological and social consequences, ACE has been associated with a wide range of adverse health outcomes in adulthood, including cardiovascular disease, metabolic disorders, mental illness, and premature mortality[11–13]. More recently, attention has focused on the association between ACE and accelerated reproductive events[14]. For instance, a US-based study by Kling et al. found no statistically significant association between ACE and age at natural menopause in a sample of 350 women[15]. In contrast, a large Chinese study of 9,674 women reported that threat-related early life adversity (e.g., physical abuse, sexual abuse) was associated with 8.6 months earlier age at natural menopause, whereas deprivation-related adversity (e.g., poverty, neglect) showed opposite associations[16]. These discrepant findings highlight critical gaps in the literature: the association between age at menopause remains inconsistent, with variations across populations, cultural contexts, and types of adversity. Moreover, most existing evidence is derived from single-cohort studies, limiting cross-population generalizability, and few have systematically examined how specific ACE types may mediate this relationship. Furthermore, whether the ACE-menopause association is modified by socioeconomic position, health behaviors, or comorbidity status has received limited attention, despite the potential for effect modification that could inform targeted intervention strategies.

Addressing these gaps requires harmonized analyses across large, well-characterized cohorts from diverse populations. The UK Biobank (UKB) and the Health and Retirement Study (HRS) offer unique advantages to address these limitations, providing large sample sizes, detailed ACE and reproductive health assessments, and complementary national contexts. Leveraging these two cohorts, this study aims to examine the association between ACE and age at menopause (including early menopause) and to explore effect modification by socioeconomic and behavioral factors. By integrating cross-national

replication and subgroup evaluation, this study provides robust evidence on the reproductive consequences of childhood adversity and identifies potential intervention targets for women experiencing ACE.

2. Methods

2.1 Study design and participants

Figure 1 shows the two primary components of the analytical framework. First, we extracted relevant data from UKB, employing multivariable linear regression models to quantify the association between ACE and age at menopause in the British population. Second, to verify the population generalizability of our findings, we selected comparable data from HRS, which included 5,163 participants with 8 ACE variables, for replication analysis in the US population.

The UK data were derived from UKB, a nationwide prospective study conducted between 2006 and 2010 across 22 assessment centers, enrolling 502,129 participants aged 37–73 years. Detailed information regarding the study's design and data collection methods can be found in previously published literature. As this was a cross-sectional analysis, we utilized baseline data for all variables. The US data were obtained from the University of Michigan Health and Retirement Study (HRS), a longitudinal panel study that surveys a nationally representative sample of approximately 20,000 American adults aged 50 years and older every two years. The HRS collects comprehensive data on health, economic status, and well-being, with detailed information available on the HRS website (https://hrs.isr.umich.edu). For this study, we used data from waves 9 to 15, which included relevant reproductive health information. Individuals who answered “Prefer not to answer” or “Do not know,” as well as those with missing data, were considered to have invalid data. Based on this criterion, the population selection process was as follows: For UKB, from 502,129 participants, individuals were progressively excluded: (1) male participants, n = 228,973; (2) those lacking valid data for age at menopause, n = 118,622; (3) those undergoing bilateral oophorectomy or hysterectomy before menopause, n = 12,107; (4) those lacking valid data for any of the ACE variables, n = 80,850. (5) those lacking valid data for covariates, n = 26,342. Finally, a total of 34,872 participants with complete information were included in the analysis (Fig. 2A). For HRS, from 42,406 participants in the HRS database between 2008 and 2020 (wave 9–15), individuals were progressively excluded: (1) male participants, n = 18,642; (2) those lacking valid data for age at menopause, n = 13,725; (3) those lacking valid data for ACE variables, n = 4, 698; (4) those lacking valid data for covariates, n = 178. Finally, a total of 5,163 participants with complete information were included in the analysis (Fig. 2B).

The HRS study protocol received ethical approval from the Institutional Review Board (IRB) of the University of Michigan Center for Health and Retirement Research. The UKB study obtained ethical clearance from the National Information Governance Board for Health and Social Care and the North West Multicenter Research Ethics Committee. This research was conducted under UK Biobank project number 280,100. All participants provided written informed consent.

2.2 Assessment of ACE

In UKB, five ACE variables, encompassing physical neglect, emotional neglect, sexual abuse, physical abuse, and emotional abuse, was assessed using the Childhood Trauma Screener, a validated instrument administered via the 2016 online mental health questionnaire[17]. Each domain was evaluated with a specific question: 1) "someone to take to doctor when needed as a child" (physical neglect); 2) "felt loved as a child" (emotional neglect); 3) "sexually molested as a child" (sexual abuse); 4) "physically abused by family as a child" (physical abuse); and 5) "felt hated by a family member" (emotional abuse) [18]. All items were prefaced with the statement: "When I was growing up (age < 16 years old)". Responses ranged from "never true" to "very often true". Based on validated cutoff points[19, 20], each item was dichotomized (0/1). Specifically, physical neglect was coded as 1 for responses of never true, rarely true, sometimes true, or often true; emotional neglect was coded as 1 for never true, rarely true, or sometimes true; sexual abuse, physical abuse, and emotional abuse were coded as 1 for responses of rarely true, sometimes true, often true, or very often true. A cumulative ACE score (range 0–5) was then calculated by summing the scores of all five types, with higher scores indicating greater exposure to childhood adversity. Due to small numbers in the highest categories, scores of 4 and 5 were combined into a single category (ACE ≥ 4). Detailed question wording and cutoff criteria are provided in Supplementary Table S1.

- In HRS, an ACE scale was constructed using eight items from the core survey and life history surveys, selected to reflect the ACE scale developed by the Centers for Disease Control and Prevention, as well as childhood socioeconomic status[21]. Specifically, participants reported on the following eight adversities: 1) parental education (both parents < high school, or one parent < high school if only one parent was reported); 2) parental physical abuse ("were you ever physically abused by either of your parents?") before age 18; 3) parental alcohol and drug use ("did either of your parents drink or use drugs so often that it caused problems in the family?") before age 18; 4) childhood separation from either parent ("were you ever separated from your mother or father for 6 months or longer?") before age 16; 5) death of a parent ("did one or both parents die?") before age 16; 6) living in a children's home or orphanage ("did you ever live in a children's home or orphanage?") before age 16; 7) childhood poverty ("would you say your family during that time was pretty well off financially, about average, or poor?"; poor = 1); and 8) parental separation or divorce ("did your biological or adoptive parents separate or divorce?") before age 16. All items referred to experiences before age 18, except for parental separation or divorce, which was assessed before age 16. To address item non-response, participants were allowed to be missing on one item (coded as 0)[21]. A cumulative ACE score was then calculated by summing the scores of all eight items. Due to small numbers in the highest categories, scores of 4 or more were top-coded into a single category (ACE ≥ 4). Detailed question wording and coding criteria are provided in Supplementary Table S2.

2.3 Assessment of age at menopause

Data on age at menopause in UKB were collected via touchscreen questionnaires under the category "Female-specific factors" (data-field 3581). Specifically, age at menopause

was determined by asking naturally menopausal women: "How old were you when your periods stopped?" Natural menopause was defined as the permanent cessation of regular menstrual periods for 12 consecutive months due to menopause, with no history of bilateral oophorectomy or hysterectomy before menopause[22]. In HRS, age at menopause was derived from the question: "About how old were you when you finished going through menopause, that is, your last menstrual period?" collected across waves 9 to 15. If responses differed across waves, the age reported at the most recent wave was used[23]. Unlike the UKB, the HRS lacked data on bilateral oophorectomy or hysterectomy; therefore, no exclusions were made based on these procedures. Given the lack of consensus on the definition of early menopause, we applied three age thresholds —40, 45, and 48 years—to define early menopause in both cohorts, thereby ensuring the robustness of the associations and facilitating comparability with previous studies[24–26].

2.4 Assessment of covariate

In both cohorts, covariates were selected based on directed acyclic graphs (DAGs) to identify potential confounders of the association between ACE and age at menopause (Figure S1). In UKB, covariates were derived from baseline measurements, whereas HRS covariates were obtained from demographics, health, employment history, and physical measures. Both datasets included the following core covariates: body mass index (BMI), income, university education, career, race/ethnicity, smoking, drinking, comorbidity, and depression. Comorbidity was defined as the presence of at least one of the following conditions: diabetes, hypertension, heart disease, cancer, cardiovascular disease, or lung disease. Additionally, in UKB, we further adjusted for the Townsend Deprivation Index (TDI), age at menarche, and live birth. Owing to differences in variable collection and classification between the two databases, as well as the smaller sample size of HRS, the adjusted covariates differed slightly; nevertheless, both models shared the same core objective of controlling for confounding factors that may influence age at menopause. Detailed covariate definitions and data sources are provided in Tables S3 and S4.

Depressive symptoms were assessed using validated instruments in both cohorts. In UKB, depression was measured between 2016 and 2017 using the Patient Health Questionnaire-9 (PHQ-9)[27, 28]. Participants rated how often they had been bothered by nine problems on a 4-point scale (0 = not at all to 3 = nearly every day), and a sum score was computed. In HRS, depressive symptoms were assessed using the eight-item Center for Epidemiologic Studies Depression Scale (CES-D8), comprising six negative items and two positive items (the latter reverse-coded)[29]. Total CES-D8 scores ranged from 0 to 8, with higher scores indicating greater depressive symptom severity.

2.5 Statistical analysis

First, we described the distribution of baseline characteristics across groups stratified by age at menopause: premature menopause (< 48 years), normal menopause (48–54 years), and delayed menopause (> 54 years). Continuous variables were presented as medians with interquartile ranges (IQR; Q1, Q3), and between-group comparisons were performed using the Kruskal–Wallis rank-sum test. Categorical variables were expressed as frequencies and percentages and were compared using Pearson's chi-square test. Next, we performed Spearman correlation analyses among the covariates and ACE variables to explore potential multicollinearity issues. To further investigate the association between ACE and age at menopause, we performed multivariable linear regression analyses in both cohorts, estimating regression coefficients (β) with 95% confidence intervals (CIs) for the exposure variable. Two models were constructed: a crude model with no covariate adjustment, and Model 1, which included adjustments for BMI, income, university education, career,

race/ethnicity, TDI (UKB only), smoking, drinking, comorbidity, depression, age at menarche (UKB only), and live birth (UKB only). Furthermore, to evaluate the relationship between ACE and early menopause (defined as age at menopause < 40, < 45, and < 48 years), we treated early menopause as a binary outcome and conducted multivariable logistic regression analyses, presenting odds ratios (ORs) with their 95% CIs, with covariate adjustments identical to those used in the linear regression models for each cohort. In addition to the cumulative ACE score, we also examined the association between each ACE component and both outcomes using the same adjustment sets.

Additionally, to assess the robustness of our findings and explore heterogeneity across subgroups, we stratified the sample by the following variables and conducted stratified analyses of the association between ACE and age at menopause: BMI (< 18.5 kg/m², 18.5–25 kg/m², 25–30 kg/m², > 30 kg/m²), income (low, medium, high), university education (yes vs. no), career (yes vs. no), ethnicity/race (White, Black, Other), TDI (low, high; UKB only), drinking status (yes vs. no), smoking status (yes vs. no), and comorbidity (yes vs. no). Subgroup definitions in the HRS were modified accordingly based on available variables (e.g., TDI was not available in HRS). Interaction analyses were also performed by introducing interaction terms between ACE and each stratification variable into the regression models, with P values for interaction calculated to assess effect modification.

All statistical analyses were conducted using R software (version 4.4.2). A two-sided P-value of < 0.05 was considered statistically significant.

3. Results

3.1 Baseline characteristics of study participants

A total of 34,872 participants from UKB and 5,163 participants from HRS were included in this study. Detailed participant characteristics are presented in Table 1. After stratifying participants into premature menopause (< 48 years), normal menopause (48–54 years), and delayed menopause (> 54 years) groups based on age at menopause, statistically significant differences across the three groups were observed in several variables, including BMI (UKB only), income, university education, career, race/ethnicity, TDI (UKB only), drinking, smoking, comorbidity, depression, live birth (UKB only), and ACE (all P < 0.05). In the UKB cohort, participants in the premature menopause group tended to have lower income, lower university education attainment, slightly lower career rate, higher TDI scores (indicating greater deprivation), and higher smoking rate. In the HRS cohort, the premature menopause group was more likely to have lower income, lower university education attainment, lower career rate, higher smoking rate, and higher comorbidity burden compared with the normal and delayed menopause groups. Overall, across both cohorts, individuals with premature menopause consistently exhibited a less favorable socioeconomic profile, including lower income, lower university education attainment, and higher smoking rates, compared with those with normal or delayed menopause. The Spearman correlation analysis showed mild to moderate correlations among the covariates and ACE variables (Figure S2)

Table 1
Baseline Characteristics of UK Biobank and US HRS Participants.

Characteristic	UKB					HRS				
	Overall N = 34872 [a]	Premature, < 48 years N = 6464 (18.5%) [a]	Normal, 48–54 years N = 22981 (65.9%) [a]	Delayed, > 54 years N = 5427 (15.6%) [a]	P [b]	Overall N = 5163 [a]	Premature, < 48 years N = 1377 (26.7%) [a]	Normal, 48–54 years N = 2616 (50.7%) [a]	Delayed, > 54 years N = 1170 (22.6%) [a]	P [b]
BMI	25.38 (23.02,28.49)	25.35 (22.85,28.56)	25.27 (22.96,28.36)	25.84 (23.45,29.03)	**< 0.001**	26.6 (23.4,31.2)	27 (23.4,31.9)	26.6 (23.4,31.02)	26.6 (23.4,30.9)	0.3
Income					**< 0.001**					**< 0.0**
Low	15165 (43.5%)	2846 (44%)	9657 (42%)	2662 (49.1%)		2921 (56.6%)	854 (62%)	1447 (55.3%)	620 (53%)	
Medium	10043 (28.8%)	1819 (28.1%)	6675 (29%)	1549 (28.5%)		1624 (31.5%)	400 (29%)	821 (31.4%)	403 (34.4%)	
High	9664 (27.7%)	1799 (27.8%)	6649 (29%)	1216 (22.4%)		618 (12%)	123 (8.9%)	348 (13.3%)	147 (12.6%)	
University education					**< 0.001**					**< 0.0**
No	17719 (50.8%)	3441 (53.2%)	11473 (49.9%)	2805 (51.7%)		2389 (46.3%)	749 (54.4%)	1162 (44.4%)	478 (40.9%)	
Yes	17153 (49.2%)	3023 (46.8%)	11508 (50.1%)	2622 (48.3%)		2774 (53.7%)	628 (45.6%)	1454 (55.6%)	692 (59.1%)	
Career					**< 0.001**					**< 0.0**
No	1344 (3.9%)	277 (4.3%)	912 (4%)	155 (2.9%)		1688 (32.7%)	516 (37.5%)	830 (31.7%)	342 (29.2%)	
Yes	33528 (96.1%)	6187 (95.7%)	22069 (96%)	5272 (97.1%)		3475 (67.3%)	861 (62.5%)	1786 (68.3%)	828 (70.8%)	
Race/ethnicity					**< 0.001**					**< 0.0**
White	34058 (97.7%)	6271 (97%)	22467 (97.8%)	5320 (98%)		3782 (73.3%)	937 (68%)	1979 (75.6%)	866 (74%)	
Black	-	-	-	-		942 (18.2%)	309 (22.4%)	408 (15.6%)	225 (19.2%)	
Other	814 (2.3%)	193 (3%)	514 (2.2%)	107 (2%)		439 (8.5%)	131 (9.5%)	229 (8.8%)	79 (6.8%)	
TDI	-2.46 (-3.82,-0.26)	-2.28 (-3.71,0.14)	-2.49 (-3.83,-0.29)	-2.55 (-3.87,-0.55)	**< 0.001**	-	-	-	-	-
Drinking										
No	1161 (3.3%)	251 (3.9%)	721 (3.1%)	189 (3.5%)	**0.01**	2342 (45.4%)	706 (51.3%)	1122 (42.9%)	514 (43.9%)	**< 0.0**
Yes	33711 (96.7%)	6213 (96.1%)	22260 (96.9%)	5238 (96.5%)		2821 (54.6%)	671 (48.7%)	1494 (57.1%)	656 (56.1%)	
Smoking					**< 0.001**					
No	20778 (59.6%)	3671 (56.8%)	13840 (60.2%)	3267 (60.2%)		2655 (51.4%)	659 (47.9%)	1356 (51.8%)	640 (54.7%)	**0.0**
Yes	14094 (40.4%)	2793 (43.2%)	9141 (39.8%)	2160 (39.8%)		2508 (48.6%)	718 (52.1%)	1260 (48.2%)	530 (45.3%)	
Comorbidity					**< 0.001**					**< 0.0**

Footnotes: Bold values indicate statistical significance (P < 0.05 or P < 0.001).

Abbreviations: UKB, UK Biobank; HRS, Health and Retirement Study; BMI, Body Mass Index; TDI, Townsend Deprivation Index; ACE, Adverse Childhood Experiences.

a Median (Q1,Q3) for continuous; n (%) for categorical.

b The P were assessed by Kruskal-Wallis test or Pearson's Chi-squared test.

Characteristic	UKB					HRS				
	Overall **N = 34872** [a]	**Premature, < 48 years** **N = 6464 (18.5%)** [a]	**Normal, 48–54 years** **N = 22981 (65.9%)** [a]	**Delayed, > 54 years** **N = 5427 (15.6%)** [a]	**P** [b]	**Overall** **N = 5163** [a]	**Premature, < 48 years** **N = 1377 (26.7%)** [a]	**Normal, 48–54 years** **N = 2616 (50.7%)** [a]	**Delayed, > 54 years** **N = 1170 (22.6%)** [a]	**P** [b]
No	15155 (43.5%)	2797 (43.3%)	10336 (45%)	2022 (37.3%)		1198 (23.2%)	260 (18.9%)	667 (25.5%)	271 (23.2%)	
Yes	19717 (56.5%)	3667 (56.7%)	12645 (55%)	3405 (62.7%)		3965 (76.8%)	1117 (81.1%)	1949 (74.5%)	899 (76.8%)	
Depression	2 (0,4)	2 (0,4)	2 (0,3)	2 (0,3)	**< 0.001**	1 (0,2)	1 (0,3)	1 (0,2)	1 (0,2)	**< 0.0**
Age at menarche	13 (12,14)	13 (12,14)	13 (12,14)	13 (12,14)	0.069	-	-	-	-	-
Live birth	2 (1,2)	2 (0,2)	2 (1,2)	2 (1,3)	**< 0.001**	-	-	-	-	-
ACE	0 (0,1)	0 (0,1)	0 (0,1)	0 (0,1)	**< 0.001**	1 (0,2)	1 (0,2)	1 (0,2)	1 (0,2)	**< 0.0**

Footnotes: Bold values indicate statistical significance (P < 0.05 or P < 0.001).

Abbreviations: UKB, UK Biobank; HRS, Health and Retirement Study; BMI, Body Mass Index; TDI, Townsend Deprivation Index; ACE, Adverse Childhood Experiences.

a Median (Q1,Q3) for continuous; n (%) for categorical.

b The P were assessed by Kruskal-Wallis test or Pearson's Chi-squared test.

3.2 Association between ACE and age at menopause

Tables 2 and 3 present the associations between ACE (both cumulative score and individual ACE components) and age at menopause (as a continuous variable) or early menopause (as a binary variable) in the UKB and US HRS cohorts, using linear and logistic regression models, respectively. In both populations, when ACE was treated as a continuous variable in the fully adjusted model (Model 1), significant negative associations were observed between ACE and age at menopause (UKB: β = -0.074, 95% CI = -0.116 to -0.032, P < 0.001; HRS: β = -0.254, 95% CI = -0.372 to -0.136, P < 0.001). Accordingly, ACE was significantly associated with increased odds of early menopause in both cohorts (UKB, < 40 years: OR = 1.141, 95% CI = 1.059 to 1.228, P < 0.001; UKB, < 45 years: OR = 1.054, 95% CI = 1.018 to 1.091, P < 0.001; UKB, < 48 years: OR = 1.044, 95% CI = 1.018 to 1.070, P < 0.001; HRS, < 40 years: OR = 1.197, 95% CI = 1.074 to 1.334, P = 0.001; HRS, < 45 years: OR = 1.102, 95% CI = 1.034 to 1.175, P = 0.003; HRS, < 48 years: OR = 1.108, 95% CI = 1.054 to 1.165, P < 0.001). When ACE was categorized by the number of adverse experience types (0 as reference), a significant dose-response relationship was observed in both populations (all P for trend < 0.001). In the UKB cohort, compared with individuals with an ACE score of 0, those with an ACE score of 4 showed the strongest association (age at menopause: β = -0.455, 95% CI = -0.692 to -0.218, P < 0.001; early menopause, < 40 years: OR = 1.813, 95% CI = 1.246 to 2.578, P = 0.001; early menopause, < 45 years: OR = 1.322, 95% CI = 1.097 to 1.583, P = 0.003; early menopause, < 48 years: OR = 1.206, 95% CI = 1.049 to 1.381, P = 0.008). In the HRS cohort, similarly, an ACE score of 4 was associated with the largest effect size (age at menopause: β = -1.200, 95% CI = -1.780 to -0.635, P < 0.001; early menopause, < 45 years: OR = 1.513, 95% CI = 1.117 to 2.032, P = 0.007; early menopause, < 48 years: OR = 1.510, 95% CI = 1.189 to 1.911, P = 0.001).

Table 2
Association between ACE and age at menopause in linear regression models, UK Biobank and US HRS.

		Age at menopause			
		Crude model		Model 1	
		β (95%CI)	P	β (95%CI)	P
UKB	**ACE**	-0.124 (-0.165, -0.083)	**< 0.001**	-0.074 (-0.116, -0.032)	**< 0.001**
	ACE level				
	0	ref		ref	
	1	-0.039 (-0.147, 0.069)	0.483	0.005 (-0.103, 0.113)	0.930
	2	-0.167 (-0.315, -0.019)	0.027	-0.056 (-0.204, 0.093)	0.463
	3	-0.365 (-0.563, -0.167)	**< 0.001**	-0.195 (-0.394, 0.005)	0.056
	≥ 4	-0.629 (-0.864, -0.394)	**< 0.001**	-0.455 (-0.692, -0.218)	**< 0.001**
	P for trend		**< 0.001**		**< 0.001**
HRS	**ACE**	-0.382 (-0.493, -0.271)	**< 0.001**	-0.254 (-0.372, -0.136)	**< 0.001**
	ACE level				
	0	ref		ref	
	1	-0.356 (-0.724, 0.013)	0.059	-0.168 (-0.538, 0.202)	0.374
	2	-1.050 (-1.460, -0.634)	**< 0.001**	-0.767 (-1.190, -0.346)	**< 0.001**
	3	-0.719 (-1.220, -0.215)	**0.005**	-0.310 (-0.825, 0.205)	0.238
	≥ 4	-1.690 (-2.240, -1.140)	**< 0.001**	-1.200 (-1.780, -0.635)	**< 0.001**
	P for trend		**< 0.001**		**< 0.001**

Footnotes: Linear regression was used for the continuous outcome, age at menopause. The crude model was an unadjusted model. In UKB Model 1, adjustments were made for BMI, income, university education, career, TDI, ethnicity/race, smoking, drinking, comorbidity, depression, age at menarche, and live birth. In HRS Model 1, adjustments were made for BMI, income, university education, career, ethnicity/race, smoking, drinking, comorbidity, and depression. The results show the regression coefficients (β), their 95% confidence intervals (95% CI), and P. Bold values indicate statistical significance ($P < 0.05$ or $P < 0.001$). P for trend indicates the statistical significance of the trend across categories of the ACE level.

Abbreviations: BMI, Body Mass Index; TDI, Townsend Deprivation Index; CI, Confidence interval; UKB, UK Biobank; HRS, Health and Retirement Study; ACE, Adverse Childhood Experiences.

Table 3
Association between ACE and early menopause defined at three age thresholds (< 40, < 45, and < 48 years) in logistic regression models, UK Biobank and US HRS.

		Early menopause (< 40 years old)				Early menopause (< 45 years old)				Early menopause (< 48 years old)			
		Crude model		Model 1		Crude model		Model 1		Crude model		Model 1	
		OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P	OR (95%CI)	P
UKB	**ACE**	1.202 (1.121, 1.289)	**< 0.001**	1.141 (1.059, 1.228)	**< 0.001**	**1.089 (1.054, 1.126)**	**< 0.001**	**1.054 (1.018, 1.091)**	**0.003**	1.076 (1.051, 1.103)	**< 0.001**	1.044 (1.018, 1.070)	**< 0.001**
	ACE level												
	0	ref		ref		ref		ref		ref		ref	
	1	1.172 (0.944, 1.449)	0.144	1.122 (0.902, 1.390)	0.294	1.061 (0.966, 1.164)	0.215	1.029 (0.936, 1.130)	0.549	1.053 (0.986, 1.125)	0.122	1.022 (0.956, 1.092)	0.520
	2	1.275 (0.956, 1.675)	0.089	1.120 (0.836, 1.481)	0.435	1.127 (0.994, 1.275)	0.059	1.047 (0.921, 1.187)	0.481	1.132 (1.036, 1.236)	**0.006**	1.058 (0.967, 1.157)	0.221
	3	1.815 (1.301, 2.474)	**< 0.001**	1.527 (1.088, 2.100)	**0.012**	1.283 (1.092, 1.499)	**0.002**	1.154 (0.978, 1.353)	0.084	1.280 (1.141, 1.433)	**< 0.001**	1.161 (1.031, 1.303)	**0.013**
	≥ 4	2.168 (1.505, 3.035)	**< 0.001**	1.813 (1.246, 2.578)	**0.001**	1.489 (1.242, 1.772)	**< 0.001**	1.322 (1.097, 1.583)	**0.003**	1.346 (1.176, 1.536)	**< 0.001**	1.206 (1.049, 1.381)	**0.008**
	P for trend		**< 0.001**		**< 0.001**		**< 0.001**		**0.001**		**< 0.001**		**0.001**
HRS	**ACE**	1.274 (1.152, 1.409)	**< 0.001**	1.197 (1.074, 1.334)	**0.001**	1.163 (1.096, 1.235)	< 0.001	1.102 (1.034, 1.175)	0.003	1.154 (1.102, 1.209)	**< 0.001**	1.108 (1.054, 1.165)	**< 0.001**
	ACE level												
	0	ref		ref		ref		ref		ref		ref	
	1	1.121 (0.738, 1.686)	0.589	0.955 (0.624, 1.448)	0.831	1.196 (0.962, 1.484)	0.106	1.077 (0.862, 1.343)	0.512	1.224 (1.040, 1.439)	**0.015**	1.127 (0.955, 1.330)	0.156
	2	1.918 (1.287, 2.843)	**0.001**	1.526 (1.010, 2.294)	**0.043**	1.684 (1.343, 2.104)	**< 0.001**	1.455 (1.151, 1.835)	**0.002**	1.551 (1.301, 1.848)	**< 0.001**	1.379 (1.149, 1.652)	**0.001**
	3	2.266 (1.441, 3.503)	**< 0.001**	1.680 (1.047, 2.654)	**0.028**	1.256 (0.935, 1.667)	0.122	1.010 (0.744, 1.358)	0.947	1.340 (1.078, 1.660)	**0.008**	1.130 (0.901, 1.413)	0.286
	≥ 4	2.266 (1.388, 3.600)	**< 0.001**	1.598 (0.949, 2.630)	0.070	1.944 (1.465, 2.560)	**< 0.001**	1.513 (1.117, 2.032)	**0.007**	1.850 (1.477, 2.312)	**< 0.001**	1.510 (1.189, 1.911)	**0.001**
	P for trend		**< 0.001**		**0.010**		**< 0.001**		**0.029**		**< 0.001**		**0.003**

Footnotes: Logistic regression was used for the binary outcome early menopause, defined at three age thresholds (< 40, < 45, and < 48 years). The crude model was an un-adjusted model. In UKB Model 1, adjustments were made for BMI, income, university education, career, TDI, ethnicity/race, smoking, drinking, comorbidity, depression, age at menarche, and live birth. In HRS Model 1, adjustments were made for BMI, income, university education, career, ethnicity/race, smoking, drinking, comorbidity, and depression. The results show the odds ratios (OR), their 95% confidence intervals (95% CI), and P. Bold values indicate statistical significance (P < 0.05 or P < 0.001). P for trend indicates the statistical significance of the trend across categories of the ACE level.

Abbreviations: BMI, Body Mass Index; TDI, Townsend Deprivation Index; CI, Confidence interval; UKB, UK Biobank; HRS, Health and Retirement Study; ACE, Adverse Childhood Experiences.

Regarding individual ACE variables (Table S5 and S6), in the UKB cohort, physical abuse, sexual abuse, and emotional abuse were significantly associated with both earlier age at menopause and increased odds of early menopause in the fully adjusted model (all P < 0.05). In the HRS cohort, death of a parent was consistently associated with both earlier menopause and increased odds of early menopause in the fully adjusted model (all P < 0.05). Other ACE components, such as parental education, parental physical abuse, childhood separation from either parent, childhood poverty, and parental separation or divorce, showed significant associations in the crude model but became non-significant after adjusting for covariates.

3.3 Subgroup analysis

Figure 3 presents the subgroup analysis results of the associations between ACE and age at menopause (as a continuous variable) in the UKB (Fig. 3A) and the US HRS (Fig. 3B) cohorts. In UKB cohort, significant negative associations between ACE and age at menopause were observed across multiple subgroups, except for “BMI < 18.5”, “25 < BMI ≤ 30” “high income”, “no career”, “low TDI”, “other ethnicity/race”, “other ethnicity/race”, “non-drinking”, and “non-smoking” individuals. In the US HRS cohort, significant negative associations were observed between ACE and age at menopause in all subgroups except for “BMI < 18.5”, “18.5 ≤ BMI ≤ 25”, “high income”, and “other ethnicity/race” individuals. Notably, interaction analyses indicated that TDI showed potential interaction effects across the UKB cohort, with stronger negative associations observed among high TDI individuals. No significant interactions were detected for any stratification variable in the HRS cohort.

4. Discussion

In this cross-national study, we found that a higher level of ACE was consistently linked to an earlier age at menopause and an increased likelihood of experiencing early menopause (< 48 years) across diverse populations. Furthermore, the strength of this association varied according to specific components of ACE: within the UKB cohort, physical abuse, sexual abuse, and emotional abuse emerged as the primary determinants, whereas in the HRS cohort, the death of a parent and living in a children's home or orphanage exhibited the strongest correlations. Subgroup analyses indicated that the negative correlation between ACE and age at menopause was broadly consistent across most demographic strata, with TDI revealing potential interaction effects in the UKB cohort. These findings offer compelling evidence that childhood adversity accelerates reproductive aging—particularly among women in socioeconomically deprived areas—suggesting important implications for targeted prevention strategies in disadvantaged communities.

Previous studies have explored the associations between ACE and earlier menopause. In a US cohort of 732 women, Allsworth et al. found that childhood or adolescent abuse was modestly associated with elevated follicle-stimulating hormone levels, suggesting potential implications for ovarian function and perimenopausal timing [30]. A Chinese study of 9,674 women reported that ≥ 3 threat-related early life adversities (e.g., physical abuse, sexual abuse) were associated with accelerated reproductive strategy, whereas cumulative deprivation was linked to delayed menopause[16]. Kling et al. observed a 1.3-year earlier natural menopause among women with ≥ 4 ACEs versus those with none in a US cohort of 350 women, though the estimate was imprecise and not statistically significant[15]. Whereas previous investigations have often been limited by small sample sizes and restricted demographic diversity, the present study leverages two large national cohorts, affording greater statistical power and cross-population generalizability. Our results broadly align with these observations while revealing notable cross-cohort heterogeneity: direct maltreatment (physical, sexual, and emotional abuse) dominated in the UKB, whereas household dysfunction and institutional care (parental death) were most salient in the HRS. This discrepancy likely reflects differences in measurement instruments—the UKB's trauma-focused screener versus the HRS's broader ACE inventory—as well as cohort-specific cultural and historical contexts that shape the nature and impact of early-life stressors. Despite these differences, the cumulative ACE score showed consistent associations across both cohorts, supporting the cumulative risk model. From a life history theory perspective, early-life adversity may accelerate reproductive timing as an adaptive strategy in response to unpredictable environments[31, 32]. The underlying neurobiological mechanisms—sustained HPA axis dysregulation, chronic inflammation, and accelerated cellular aging—provide a plausible unifying pathway through which diverse forms of childhood adversity converge to influence ovarian aging[33, 34].

In the UKB cohort, a significant interaction was observed between ACE and the area-level TDI, whereby women residing in more socioeconomically deprived neighborhoods exhibited stronger negative associations between ACE and age at menopause. This pattern supports the stress sensitization hypothesis, which posits that early-life adversity may lower physiological thresholds for responding to subsequent environmental stressors, thereby amplifying vulnerability to cumulative socioeconomic hardship encountered in later life[35]. The underlying pathways likely involve sustained HPA axis dysregulation, chronic low-grade inflammation, accelerated telomere attrition, and epigenetic alterations—mechanisms that are independently associated with both childhood maltreatment and chronic neighborhood stress, and may converge to accelerate ovarian follicular depletion[36–38]. Area-level deprivation, as captured by the TDI, reflects not only material resource scarcity but also broader contextual factors such as neighborhood safety, social cohesion, physical infrastructure, and environmental exposures[39], all of which contribute to allostatic load and may compound the neuroendocrine sequelae of early adversity. In contrast, the attenuated associations observed among high-income individuals are consistent with the stress-buffering model[40], wherein greater individual-level socioeconomic resources—facilitating access to preventive care, better nutrition, and reduced psychosocial stress—may offset the reproductive consequences of ACE[41, 42]. Collectively, these findings suggest that both neighborhood-level socioeconomic context and individual-level resources moderate the impact of early-life stress on reproductive aging, underscoring the importance of adopting a multi-level socioecological perspective in future investigations of women's reproductive health.

This study has several notable methodological strengths. First, the harmonized analytical approach across two large, nationally representative cohorts from the UK and the US enabled cross-validation and enhanced the generalizability of our findings across different healthcare systems, cultural contexts, and population characteristics. Besides, the availability of detailed ACE measures in both cohorts—including cumulative scores and individual component data—allowed us to examine dose-response relationships and disaggregate the effects of specific types of adversity. Moreover, the inclusion of extensive covariate information permitted rigorous adjustment for potential confounders, and the consistency of results across linear and logistic regression frameworks, as well as across crude and fully adjusted models, supports the stability of our estimates. Finally, the subgroup analyses with formal interaction testing enabled systematic evaluation of effect modification by socioeconomic and behavioral factors, providing a comprehensive analytical framework for assessing heterogeneity across population strata. Nevertheless, several limitations warrant consideration. First, the cross-sectional design of both studies precludes causal inference; although we observed significant associations, prospective studies are needed to establish temporality and confirm causal pathways. Second, ACEs and age at menopause were self-reported, raising the possibility of recall bias, though previous validation studies have shown acceptable reliability of retrospective ACE reports, and the consistency of associations across cohorts mitigates concerns about differential misclassification. Furthermore, the HRS lacked enough data on bilateral oophorectomy and hysterectomy, which may have led to residual confounding or misclassification of natural menopause. Additionally, although the ACE instruments differed between cohorts—with UKB using a 5-item trauma screener and HRS using an 8-item

ACE scale—it is noteworthy that the direction and significance of the core associations were consistent across both cohorts. This cross-cohort concordance, despite measurement heterogeneity, strengthens confidence in the robustness of our main findings. Finally, the study populations were predominantly White (UKB: 97.7%; HRS: 73.3%), limiting generalizability to other racial/ethnic groups.

Our findings raise several questions for future investigation. Prospective studies with repeated assessments of ACEs and reproductive outcomes are needed to establish temporal sequence and causal pathways. Alongside this, research examining the biological and psychological mechanisms linking childhood adversity to ovarian aging—such as telomere attrition, oxidative stress, HPA axis dysregulation, and depressive disorders—could provide deeper insights into the underlying pathophysiology. Equally important, future studies should include more diverse populations to determine whether the ACE–menopause association varies by race/ethnicity, socioeconomic status, or cultural context. Finally, research exploring the long-term health consequences of ACE-associated early menopause—including cardiovascular disease, osteoporosis, and cognitive decline—could inform clinical monitoring and prevention strategies.

Our findings carry several clinical and public health implications. At the clinical level, screening for childhood adversity—particularly in socioeconomically deprived areas, where the ACE–menopause association was strongest—may help identify women at elevated risk for accelerated reproductive aging, enabling earlier reproductive life planning and monitoring of menopause-related outcomes. Healthcare systems serving disadvantaged populations should consider integrating ACE screening and depression monitoring into routine reproductive health services for women presenting with early menopause or related concerns. At the population level, the consistency of findings across two large, nationally representative cohorts from the UK and the US supports the generalizability of these associations, reinforcing that childhood adversity is a relevant reproductive health determinant across different healthcare and cultural contexts. At the societal level, our findings underscore the importance of broader strategies to prevent childhood maltreatment. Beyond clinical screening, public health efforts should focus on raising awareness about the lifelong health consequences of child abuse and neglect—including reproductive health—and strengthening support systems for at-risk families. For parents and caregivers, this study serves as an important reminder that protecting children from abuse and neglect is not only a moral and legal obligation but also essential for their long-term physical health, with effects that may not become apparent until decades later. Greater public awareness, early intervention, and family support programmes are essential to break the cycle of adversity and safeguard the health of future generations.

5. Conclusion

In this large cross-national study, ACE was consistently associated with earlier menopause and increased odds of early menopause across both cohorts, with a significant dose-response relationship. Although the specific ACE components driving these associations differed by cohort, the overall convergence supports a robust link between childhood adversity and reproductive aging. Subgroup and interaction analyses confirmed the robustness of these findings across most strata and further revealed that area-level socioeconomic deprivation—as measured by the Townsend Deprivation Index—may intensify the adverse effects of ACE, particularly among women residing in disadvantaged neighborhoods. Further research is needed to assess whether routine ACE screening in clinical practice can help identify at-risk women and inform preventive strategies, particularly in socioeconomically deprived communities where the burden may be greatest.

Declarations

Ethics approval and consent to participate

This study utilized publicly available data from the Health and Retirement Study (HRS) and the UK Biobank. HRS: Approved by the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board (no public protocol number required for public-use data). UK Biobank: Project ID: 280,100. As secondary users of these de-identified public-use datasets, we conducted all analyses in accordance with the data access agreements and ethical governance frameworks of the respective databases, as well as the general principles for ethical secondary research outlined in the Declaration of Helsinki (for observational studies).

Consent for publication

Not applicable. The data for this study were obtained from public databases.

Competing Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Author Contribution

Weiqian Zhang: Formal analysis, Visualization, Writing-original draft, Writing-review&editing. Yiling Tan: Writing-original draft, Writing-review&editing. Rui Qu: Writing-original draft, Writing-review&editing. Jia Liang: Investigation, Writing-review&editing. Yu Guan: Data curation, Writing-review&editing. Tailang Yin: Funding acquisition, Writing-review & editing. Dongdong Tang: Conceptualization, Project administration, Funding acquisition, Supervision, Writing-review&editing. Yan Zhang: Funding acquisition, Writing-review&editing.

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During the preparation of this work, the authors utilized AI-assisted tools ChatGPT and DeepSeek to enhance the manuscript's readability and language quality. After using these tools, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

Availability of data and materials

The UK Biobank data can be accessed upon application through the official website: www.ukbiobank.ac.uk.

The HRS data are available for download at: https://hrsdata.isr.umich.edu/data-products.

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Figures

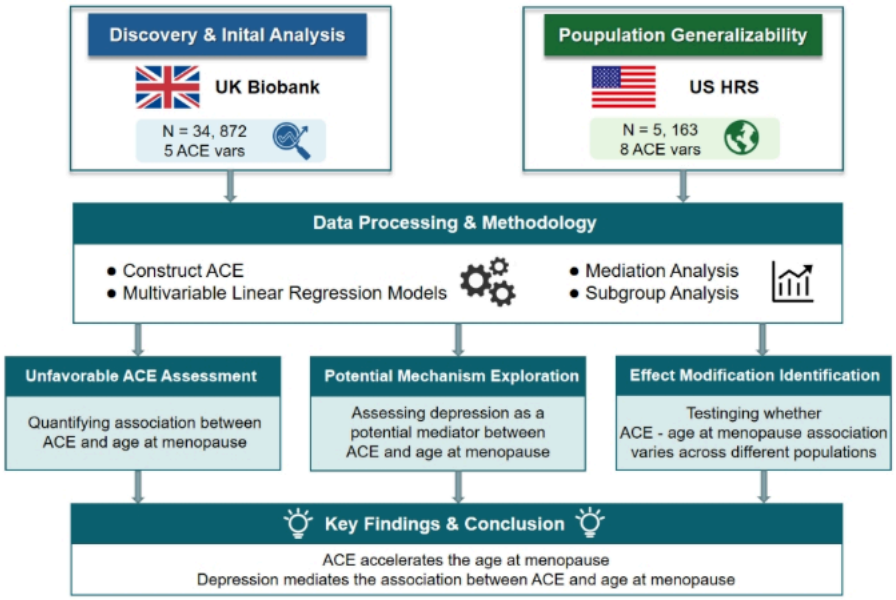


Figure 1

The overview of this study. Abbreviations: ACE, Adverse Childhood Experiences; HRS, Health and Retirement Study.

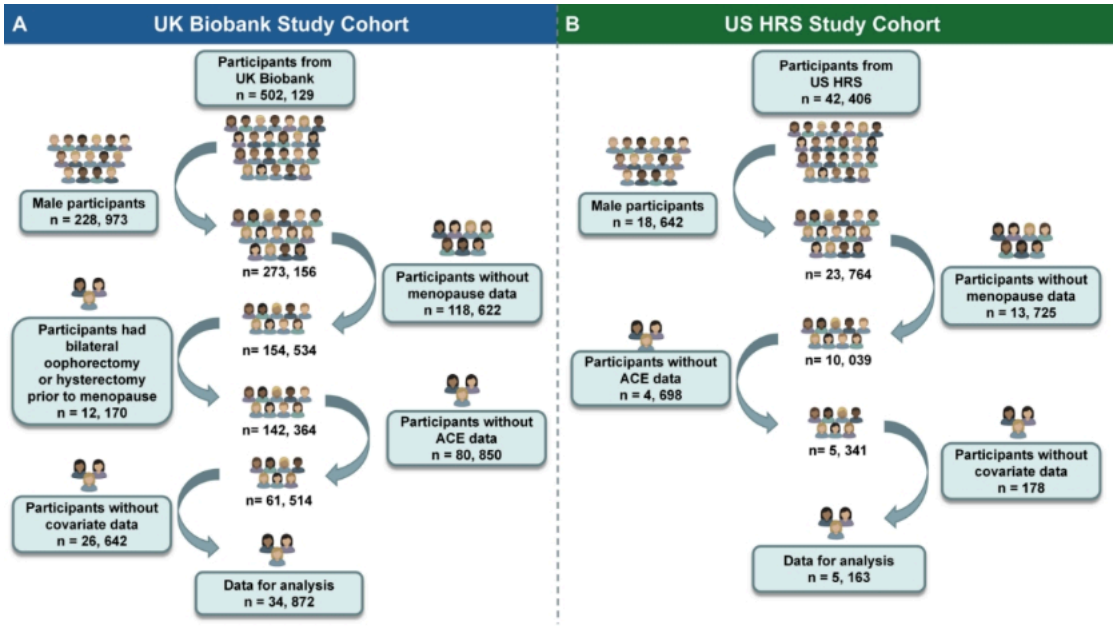


Figure 2

Flowchart of study population selection. A. UK Biobank; B. US HRS

Abbreviations: HRS, Health and Retirement Study; ACE, Adverse Childhood Experiences.

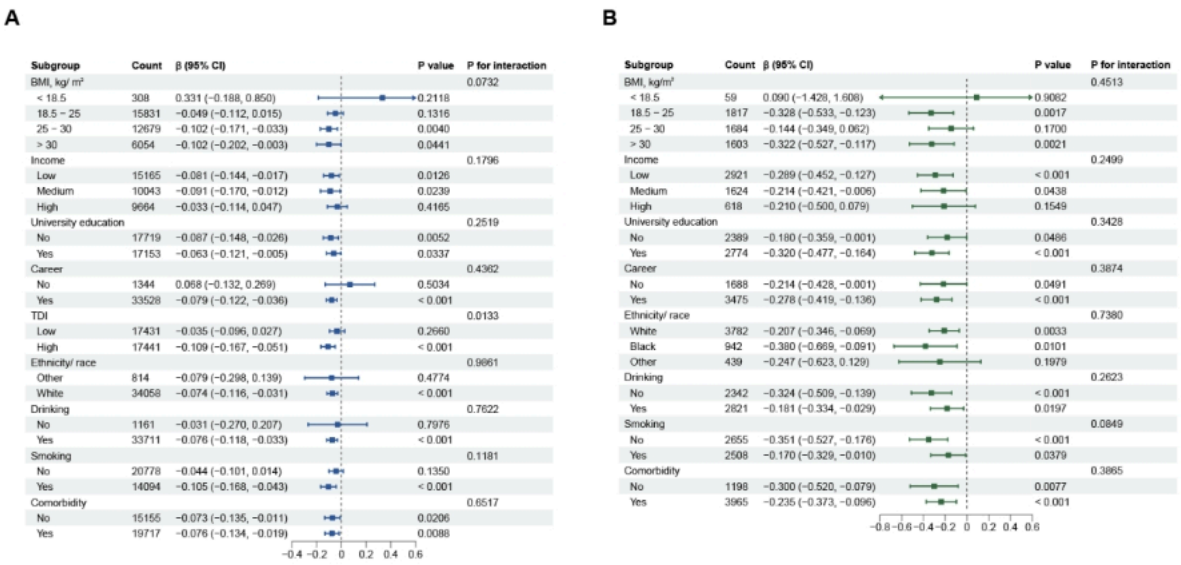


Figure 3

Subgroup analysis of the association between ACE and age at menopause. (A) UK Biobank; (B) US HRS. Each subgroup analysis adjusted for all covariates except the stratification variable. In UK Biobank, adjustments were made for BMI, income, university education, career, TDI, ethnicity/race, smoking, drinking, comorbidity, as well as depression, age at menarche, and live birth, which were consistently included as covariates across all models. In US HRS, adjustments were made for BMI, income, university education, career, ethnicity/race, smoking, drinking, comorbidity, as well as depression, consistently included as covariate across all models. Abbreviations: BMI, Body Mass Index; β, regression coefficients; CI, Confidence Interval; TDI, Townsend Deprivation Index; ACE, Adverse Childhood Experiences.

Supplementary Files

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