Maturitas 129 (2019) 6–11

Contents lists available at ScienceDirect

Maturitas

journal homepage: www.elsevier.com/locate/maturitas

Associations of parental ages at childbirth with healthy aging among women

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ARTICLE INFO

Keywords:
Childbirth
Aging
Longevity
Maternal age
Paternal age
Women

ABSTRACT

Objective: To examine associations of parental ages at childbirth with healthy survival to age 90 years among older women.
Study Design: This study included a racially and ethnically diverse sub-cohort of 8,983 postmenopausal women from the larger Women's Health Initiative population, recruited during 1993–1998 and followed for up to 25 years through 2018.
Main Outcome Measures: The outcome was categorized as: 1) healthy survival, defined as survival to age 90 without major morbidities (coronary heart disease, stroke, diabetes, cancer, or hip fracture) or mobility disability; 2) usual survival, defined as survival to age 90 without healthy aging (reference category); or 3) death before age 90. Women reported their own and their parents' birth years, and parental ages at childbirth were calculated and categorized as < 25, 25–29, 30–34, or ≥35 years.
Results: Women were aged on average 71.3 (standard deviation 2.7; range 65–79) years at baseline. There was no significant association of maternal age at childbirth with healthy survival to age 90 or death before age 90. Women born to fathers aged ≥35 compared with 30–34 years at their births were more likely to achieve healthy than usual survival (OR, 1.15; 95% CI, 1.00–1.32). There was no association of paternal age at childbirth with death before age 90.
Conclusions: Findings suggest that being born to older fathers was associated with healthy survival to age 90 among women who had survived to ages 65–79 years at study baseline. There was no association of maternal age at childbirth with healthy survival to age 90 among these older women.

1. Introduction

Maternal and paternal ages at childbirth have been rising during the past four decades in the United States [1–3]. Average maternal age at first childbirth rose from 21.4 years in 1970 to 26.3 years in 2014 [1,2]. Average paternal age at childbirth increased from 27.4 years to 30.9 years during this time [3]. The proportion of births to parents older than 35 years is also increasing [1–3]. The desire to further one's education and start a family after establishing one's professional career may influence the decision to have a child at an older age [2].

Studies examining associations of parental ages at childbirth with offspring health outcomes have yielded inconsistent findings, and few studies have examined aging outcomes [4–16]. Some studies have linked older parental age at childbirth to outcomes including neurodevelopmental disorders, obesity, mortality, and morbidities including cancer among offspring in childhood and adulthood [4,9–12,14].

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https://doi.org/10.1016/j.maturitas.2019.08.002
Received 28 April 2019; Received in revised form 29 June 2019; Accepted 6 August 2019

There is some evidence that older paternal age at childbirth may confer health benefits among offspring. For example, older paternal age at childbirth has been associated with longer telomere length among adult offspring [17,18]. Shortened telomere length is associated with decreased lifespan and increased risks of cancer, cardiovascular diseases, and type 2 diabetes among adults [19–22]. However, the hypothesis that older paternal age at childbirth is associated with healthy survival to an advanced age among offspring has not, to our knowledge, been yet examined in a large, epidemiologic study with follow-up into late ages.

We examined associations of parental ages at childbirth with healthy aging, defined as survival to age 90 without major morbidities or mobility disability, among participants in the Women's Health Initiative (WHI), a large, national, prospective study of postmenopausal women in the United States.

2. Methods

2.1. Study population and design

Details of the WHI study design and population are described elsewhere [23]. Briefly, 161,808 postmenopausal women aged 50–79 years were recruited from 40 United States clinical centers from 1993 to 1998 to participate in one or more of three clinical trials or an observational study. In 2005, 77% of eligible women agreed to be followed through 2010 in the first WHI Extension Study. In 2010, 87% of eligible women enrolled for an additional five years of follow-up in the second Extension Study. Follow-up is now continuing at least through 2020. All participants provided written informed consent, and institutional review board approval was received by all participating institutions.

This study was restricted to participants born on or before March 31, 1928 who had potential, because of their birth years, to survive to age 90 during the follow-up period ending March 31, 2018. During the second Extension Study, women were asked to report the year in which their mothers and fathers were born. Women who had complete information on parental ages at childbirth, survival status, and mobility status if survived to age 90 were included in the present study. A subcohort of 8983 women with up to 25 years of follow-up met the inclusion criteria (Supplementary Figure 1).

2.2. Parental ages at childbirth

Parental ages at childbirth were determined by subtracting the self-reported parental birth years from the participant birth year and categorized as follows: < 25, 25–29, 30–34, and ≥35 years. Teen births were not examined as a separate category due to low numbers of parental ages at childbirth ≤19 years. Older parental age at childbirth was considered ≥35 years, because sociodemographic trends indicate that the number of first births in this age group is increasing among men and women [1–3]. Further, there were fewer women whose mothers or fathers were aged ≥40 compared with < 40 years at their births. Henceforth, maternal and paternal ages refer to a woman's mother's and father's ages at her own birth, respectively.

2.3. Covariates

Covariates collected at baseline included age, race/ethnicity, education, income, marital status, smoking, alcohol consumption, diet quality, body mass index (BMI), total leisure-time physical activity, depressive symptoms, and self-rated health. Additional information on these variables is provided in the Supplementary Methods.

2.4. Outcome

Participants were classified as having survived to age 90 or died before this age. Deaths were verified by physician adjudication using hospital records, autopsy or coroner's reports, or death certificates. Periodic linkage to the National Death Index was performed for all participants, including those lost to follow-up, for verification if medical records or death certificates were not available.

In prior studies, definitions of healthy aging were based on Rowe and Kahn's model, which is characterized by avoidance of major diseases and disabilities [24,25]. In the present study, healthy aging was defined as survival to ≥90 years without a history of major morbidities (coronary heart disease, stroke, cancer, diabetes, or hip fracture) or mobility disability, which was determined using the physical function subscale of the RAND 36-item health survey [26]. Women who reported needing crutches, a walker, or a wheelchair to walk on a level surface or who self-reported on the physical function subscale that their health greatly limited their ability to walk one block or climb one flight of stairs were characterized as having mobility disability [24]. The questionnaire that was collected within 2 years of the 90th birth year and with the least missing data for physical function was used. Information on collection of physician-adjudicated morbidities is provided in the Supplementary Methods.

The aging outcome variable had three categories, similar to previous studies: healthy survival (survived to age 90 and met the definition of healthy aging); usual survival (survived to age 90 but did not meet the definition of healthy aging); and died before age 90 [24,25].

2.5. Statistical analysis

Baseline characteristics were compared by parental ages using chi-square tests for categorical variables, and analysis of variance and Kruskal-Wallis tests for normally-distributed and non-normally distributed continuous variables, respectively.

The analytic approach for this study was similar to that from previous studies examining factors associated with aging outcomes [24,25]. Multinomial logistic regression models examined associations of maternal and paternal ages with the aging outcome. The reference category for maternal age at childbirth was 25–29 years and that for paternal age at childbirth was 30–34 years, which include the current average maternal (26.3 years) and paternal (30.9 years) ages at childbirth in the United States, respectively [1,3]. Usual survival was the reference category for the aging outcome. Multivariable models were adjusted for potential confounders including age at baseline, study assignment (Clinical Trial or Observational Study), race/ethnicity, education, income, marital status, smoking, alcohol consumption, BMI, physical activity, diet quality, depressive symptoms, and self-rated health. Linear trend associations were evaluated by examining parental ages as continuous predictors in the models. Results are reported as odds ratios (OR) and 95% confidence intervals (CI).

In sensitivity analyses, multivariable models for maternal age adjusted for paternal age and vice versa; an interaction between parental ages was also evaluated. Because there is no universal definition of healthy aging, examination of an alternative definition for mobility disability evaluated the robustness of our findings. Women who reported that their health greatly limited their ability to walk one block or climb one flight of stairs were classified as having mobility disability; otherwise, they had intact mobility. Finally, models were adjusted for number of brothers and sisters to determine whether family size confounded any associations between parental ages and the aging outcome.

P-values were two-tailed and considered significant at $P < 0.05$. Analyses were performed using SAS Version 9.4 (SAS Institute, Cary, NC).

3. Results

Women's average age at baseline was 71.3 (standard deviation 2.7; range, 65–79) years. Among the overall cohort, 33.4% had healthy survival to age 90, 58.9% had usual (i.e., not healthy) survival to age 90, and 7.7% died before age 90. Overall, 32.1%, 31.8%, 20.3%, and

Table 1
Baseline characteristics by maternal age at childbirth, Women's Health Initiative (N = 8833).

Characteristic	Maternal age at childbirth, years				P-value
	< 25 (n = 2833)	25-29 (n = 2809)	30-34 (n = 1795)	≥35 (n = 1396)	
Age, mean (SD), years	71.3 (2.7)	71.2 (2.6)	71.2 (2.6)	71.3 (2.7)	0.20
Race/ethnicity					
White	2602 (92.0)	2667 (95.0)	1710 (95.4)	1333 (95.6)	
Black	106 (3.8)	55 (2.0)	35 (2.0)	23 (1.7)	< 0.001
Hispanic	35 (1.2)	25 (0.9)	7 (0.4)	12 (0.9)	
Other	85 (3.0)	60 (2.1)	40 (2.2)	27 (1.9)	
Educational level					
Less than high school	113 (4.0)	62 (2.2)	37 (2.1)	44 (3.2)	
High school	515 (18.3)	405 (14.5)	251 (14.1)	245 (17.6)	< 0.001
Some college	1207 (42.8)	967 (34.6)	640 (35.8)	485 (34.9)	
College graduate	985 (34.9)	1361 (48.7)	859 (48.1)	617 (44.4)	
Income					
< $20,000	484 (18.2)	350 (13.3)	230 (13.6)	200 (15.2)	
$20,000- < $50,000	1410 (53.0)	1405 (53.4)	885 (52.2)	695 (52.9)	< 0.001
≥$50,000	766 (28.8)	875 (33.3)	580 (34.2)	418 (31.8)	
Marital status					
Married/living as married	1670 (59.2)	1700 (60.7)	1066 (59.6)	841 (60.4)	
Widowed	799 (28.3)	729 (26.0)	463 (25.9)	393 (28.2)	< 0.001
Divorced/separated	275 (9.7)	287 (10.3)	163 (9.1)	95 (6.8)	
Never married	78 (2.8)	85 (3.0)	98 (5.5)	63 (4.5)	
Smoking behavior					
Never smoked	1714 (61.3)	1579 (56.8)	1041 (58.6)	809 (58.6)	
Past smoker	1024 (36.6)	1145 (41.2)	705 (39.7)	534 (38.7)	0.01
Current smoker	60 (2.1)	56 (2.0)	31 (1.7)	38 (2.8)	
Alcohol intake					
Nondrinker	290 (10.3)	231 (8.3)	177 (9.9)	161 (11.6)	
Past drinker	472 (16.8)	425 (15.2)	257 (14.4)	183 (13.2)	< 0.001
Current drinker	2051 (72.9)	2141 (76.6)	1351 (75.7)	1048 (75.3)	
Recreational physical activity, mean (SD), MET-hours/week	12.9 (12.7)	14.1 (13.4)	14.4 (13.9)	14.8 (14.1)	< 0.001
Healthy eating index score, mean (SD)	69.5 (10.0)	70.3 (9.9)	70.3 (9.9)	69.8 (9.9)	0.007
Body mass index, kg/m^2					
Normal weight	1038 (37.2)	1118 (40.3)	809 (45.9)	537 (39.1)	
Overweight	1110 (39.7)	1070 (38.6)	615 (34.9)	548 (39.9)	< 0.001
Obese	646 (23.1)	584 (21.1)	338 (19.2)	289 (21.0)	
Burnham depression scale score ≥0.06	159 (5.7)	133 (4.8)	95 (5.4)	69 (5.1)	0.50
History of major morbidities					
Coronary heart disease	240 (8.5)	239 (8.5)	150 (8.4)	120 (8.6)	1.00
Stroke	208 (7.3)	203 (7.2)	124 (6.9)	92 (6.6)	0.81
Cancer	723 (25.5)	733 (26.1)	461 (25.7)	368 (26.4)	0.93
Diabetes	459 (16.2)	442 (15.7)	246 (13.7)	207 (14.8)	0.11
Hip fracture	226 (8.0)	224 (8.0)	143 (8.0)	118 (8.5)	0.95
≥1 disease	1403 (49.5)	1431 (50.9)	892 (49.7)	694 (49.7)	0.71
Self-rated health					
Excellent	489 (17.4)	581 (20.9)	401 (22.4)	282 (20.4)	
Very good	1382 (49.2)	1334 (47.9)	879 (49.2)	692 (50.0)	< 0.001
Good	834 (29.7)	768 (27.6)	460 (25.7)	370 (26.8)	
Fair/poor	107 (3.8)	101 (3.6)	47 (2.6)	39 (2.8)	

Data are presented as no. (%), unless otherwise indicated.

15.8% were born to mothers aged < 25, 25–29, 30–34, and ≥35 years at their births, respectively. Further, 14.2%, 29.9%, 25.3%, and 30.6% were born to fathers aged < 25, 25–29, 30–34, and ≥35 years at their births, respectively.

Women born to younger mothers were less likely to be white, college graduates, never married, or normal weight, or have high income or excellent self-rated health (Table 1). Similar relationships were observed for baseline characteristics according to paternal age (Table 2).

Among this cohort of women ages 65–79 years at baseline, maternal age was not associated with healthy survival to age 90 or death before age 90, adjusting for age, race/ethnicity, study component, education, income, marital status, smoking, alcohol consumption, diet quality, BMI, depressive symptoms, physical activity, and self-rated health (Table 3). Maternal age was not linearly associated with healthy survival to age 90 or death before age 90.

Women born to fathers aged ≥35 compared with 30–34 years had higher odds (OR, 1.15; 95% CI, 1.00–1.32) of healthy compared with usual survival to age 90 in the multivariable model (Table 3). Younger paternal age categories were not associated with healthy survival, and no linear association was observed. Paternal age was not associated with death before age 90, and a linear association was not observed among this cohort of older women.

There were no appreciable changes in findings after adjustment for maternal age in models for paternal age or vice versa; further, there was no interaction between parental ages. Findings were also similar after adjusting for number of brothers and sisters (data not shown). Using an alternative definition of mobility disability, findings for maternal age were similar (data not shown), and being born to a father aged ≥35 compared with 30–34 years at childbirth remained associated with higher odds of healthy compared with usual survival (OR, 1.19; 95% CI, 1.04,1.36).

4. Discussion

In a large, national study of postmenopausal women ages 65–79 years at study entry, those who were born to fathers aged ≥35 compared with 30–34 years at their births had higher odds of survival to age 90 without major morbidities or mobility disability, independent of

Table 2
Baseline characteristics by paternal age at childbirth, Women's Health Initiative (N = 8553).

Characteristic	Paternal age at childbirth, years				P-value
	< 25 (n = 1218)	25-29 (n = 2558)	30-34 (n = 2163)	≥35 (n = 2614)	
Age, mean (SD), years	71.4 (2.7)	71.2 (2.6)	71.2 (2.7)	71.3 (2.6)	0.16
Race/ethnicity					
White	1128 (92.7)	2438 (95.4)	2060 (95.4)	2451 (93.9)	
Black	50 (4.1)	52 (2.0)	38 (1.8)	48 (1.8)	< 0.001
Hispanic	10 (0.8)	24 (0.9)	18 (0.8)	24 (0.9)	
Other	29 (2.4)	42 (1.6)	43 (2.0)	88 (3.4)	
Educational level					
Less than high school	55 (4.5)	62 (2.4)	47 (2.2)	68 (2.6)	
High school	236 (19.4)	406 (15.9)	300 (14.0)	426 (16.4)	< 0.001
Some college	520 (42.8)	970 (38.0)	782 (36.4)	923 (35.5)	
College graduate	403 (33.2)	1113 (43.6)	1021 (47.5)	1187 (45.6)	
Income					
< $20,000	212 (18.7)	362 (15.0)	272 (13.4)	355 (14.5)	
$20,000- < $50,000	596 (52.4)	1294 (53.5)	1064 (52.3)	1313 (53.8)	0.001
≥$50,000	329 (28.9)	762 (31.5)	700 (34.4)	775 (31.7)	
Marital status					
Married/living as married	764 (62.9)	1518 (59.6)	1313 (60.8)	1538 (59.1)	
Widowed	319 (26.3)	695 (27.3)	581 (26.9)	700 (26.9)	< 0.001
Divorced/separated	107 (8.8)	258 (10.1)	178 (8.2)	237 (9.1)	
Never married	24 (2.0)	77 (3.0)	88 (4.1)	128 (4.9)	
Smoking behavior					
Never smoked	746 (62.0)	1485 (58.9)	1261 (58.8)	1509 (58.3)	
Past smoker	434 (36.1)	976 (38.7)	852 (39.7)	1021 (39.5)	0.11
Current smoker	24 (2.0)	61 (2.4)	32 (1.5)	58 (2.2)	
Alcohol intake					
Nondrinker	123 (10.2)	244 (9.6)	204 (9.5)	256 (9.8)	
Past drinker	196 (16.2)	386 (15.2)	314 (14.6)	379 (14.6)	0.83
Current drinker	892 (73.7)	1913 (75.2)	1636 (76.0)	1966 (75.6)	
Recreational physical activity, mean (SD), MET-hours/week	12.9 (13.0)	13.4 (13.0)	14.4 (14.0)	14.3 (13.6)	< 0.001
Healthy eating index score, mean (SD)	69.3 (10.1)	69.5 (10.1)	70.3 (9.8)	70.2 (9.7)	0.003
Body mass index, kg/m^2					
Normal weight	429 (35.5)	1027 (40.8)	884 (41.6)	1050 (40.8)	
Overweight	491 (40.6)	968 (38.4)	785 (37.0)	988 (38.4)	0.02
Obese	289 (23.9)	523 (20.8)	454 (21.4)	533 (20.7)	
Burnham depression scale score ≥0.06	69 (5.8)	130 (5.2)	100 (4.7)	131 (5.1)	0.61
History of major morbidities					
Coronary heart disease	92 (7.6)	208 (8.1)	179 (8.3)	239 (9.1)	0.35
Stroke	93 (7.6)	167 (6.5)	167 (7.7)	177 (6.8)	0.32
Cancer	290 (23.8)	665 (26.0)	559 (25.8)	699 (26.7)	0.29
Diabetes	188 (15.4)	402 (15.7)	334 (15.4)	376 (14.4)	0.57
Hip fracture	103 (8.5)	201 (7.9)	171 (7.9)	213 (8.2)	0.92
≥1 disease	579 (47.5)	1272 (49.7)	1108 (51.2)	1320 (50.5)	0.20
Self-rated health					
Excellent	228 (18.9)	499 (19.7)	471 (21.9)	525 (20.3)	
Very good	581 (48.1)	1217 (48.0)	1061 (49.3)	1287 (49.7)	0.007
Good	348 (28.8)	717 (28.3)	571 (26.5)	705 (27.2)	
Fair/poor	50 (4.1)	104 (4.1)	50 (2.3)	75 (2.9)	

Data are presented as no. (%), unless otherwise indicated.

age, race/ethnicity, socioeconomic status (SES), lifestyle behaviors, BMI, family size, and health-related factors. There was no association between a woman's mother's age at her birth and healthy survival to age 90, and parental ages were not associated with death before age 90 in this cohort of older women.

Associations of parental ages with childhood and adulthood health outcomes among offspring have been mixed, and few studies have examined aging outcomes, such as exceptional longevity or healthy aging [4–16]. A prospective study among > 5000 adults ages 65 years and older observed no associations of parental ages with mortality or frailty in old age among sons or daughters [7]. However, that study did not examine survival to an advanced age (i.e., longevity) or use a composite definition of healthy aging as we did in our study. Previous studies have observed no differences in paternal age between children of centenarians and controls [6,13]; however, these studies relied upon use of historical or registry-based data and did not conduct prospective studies among large cohorts of participants.

Parental age has been linked to both negative and positive health outcomes among offspring. In the Health and Retirement study, there were U-shaped associations of maternal age with mortality, self-rated heath, obesity, and number of chronic diseases, with worse outcomes for ages < 25 and > 35 compared with 25–34 years [9]; however, paternal age was not examined. Other studies have observed associations of older maternal age with offspring childhood morbidity [11], higher adult BMI [5], and higher adult blood pressure [5], as well as positive outcomes including reduced abdominal fat and improved insulin sensitivity among children [8]. Older paternal age has been associated with increased risk of non-Hodgkin's Lymphoma among women [12], obesity in adulthood [14], psychiatric morbidities in childhood and adolescence [4], and mortality [10]. Furthermore, older paternal age has been associated with increased risk of low birthweight and premature birth in some studies [15], whereas others have observed no associations of paternal age with adverse birth outcomes [16].

Unlike other studies, we examined an older, healthier cohort of women ages 65–79 years at baseline who had already survived many earlier negative outcomes that may be associated with delayed parental age. It is possible that older paternal age may be associated with adverse health outcomes earlier in life and also with healthy survival later

Table 3
Associations of parental ages at childbirth with aging outcomes, Women's Health Initiative.

	Healthy survival to age 90 vs. usual survival to age 90[a]		Death before age 90 vs. usual survival to age 90	
	No. survived to age 90 with healthy aging/total (%)	Multivariable-adjusted[b,c]OR (95% CI)	No. died before age 90/ total (%)	Multivariable-adjusted[b,c]OR (95% CI)
Maternal age at childbirth, years				
< 25	969/2833 (34.2)	1.09 (0.96-1.24)	208/2833 (7.3)	0.90 (0.71-1.14)
25-29	920/2809 (32.8)	1.00	216/2809 (7.7)	1.00
30-34	600/1795 (33.4)	1.00 (0.87-1.16)	151/1795 (8.4)	1.13 (0.88-1.46)
≥35	460/1396 (33.0)	1.02 (0.87-1.19)	98/1396 (7.0)	0.88 (0.66-1.18)
Paternal age at childbirth, years				
< 25	420/1218 (34.5)	1.15 (0.97-1.37)	96/1218 (7.9)	0.94 (0.69-1.29)
25-29	863/2558 (33.7)	1.14 (0.99-1.30)	186/2558 (7.3)	0.87 (0.68-1.13)
30-34	690/2163 (31.9)	1.00	173/2163 (8.0)	1.00
≥35	885/2614 (33.9)	1.15 (1.00-1.32)	193/2614 (7.4)	0.95 (0.74-1.22)

CI, confidence interval; OR, odds ratio.
[a] Healthy survival defined as: survival to age 90 without major morbidities (coronary heart disease, stroke, cancer, diabetes, or hip fracture) or mobility disability.
[b] Multivariable model adjusted for adjusted for age, race/ethnicity, study component (Observational Study or Clinical Trial), education, income, marital status, smoking, alcohol consumption, diet quality, body mass index, depressive symptoms, physical activity, and self-rated health.
[c] *P*-values for trend (maternal age): 0.26 (healthy survival); 0.67 (death); *P*-values for trend (paternal age): 0.87 (healthy survival); 0.65 (death).

in life, conditional upon survival to a benchmark such as 65 years. Further studies following women from ages younger than 65 years are needed to confirm these observations.

Previous studies have reported associations of older paternal age with longer offspring telomere length, supporting a potential biological mechanism for our findings [17,18]. For example, in the Nurses' Health Study, older paternal, but not maternal, age was associated with longer offspring telomere length after controlling for confounders including age and childhood SES among women [17]. Shortened telomere length is associated with reduced longevity, chronic diseases, and functional limitations, suggesting that telomere length might be a mediator in the association of paternal age with healthy aging [19–22,27]. However, we lacked adequate telomere measurements in our study population, and further studies are needed to evaluate any potential links between paternal age, telomere length, and aging outcomes.

The association of older paternal age with healthy aging may also be partly explained by residual confounding due to childhood SES. Education, employment, and wealth improve as age increases; therefore, children of older fathers tend to have greater access to economic resources [28]. We did not have information on childhood SES (e.g., father's occupation), which is associated with health outcomes in adulthood [29]. However, SES in childhood predicts SES later in life, such that older adults with higher incomes had parents who were financially well-off [30]. Because our findings were independent of SES later in life, it is possible that SES throughout the life course does not fully explain our findings.

Our study has several limitations. Parental age was not collected at the baseline visit but later during the WHI Extension Study. Therefore, our study population consisted of an older cohort of women who lived long enough and agreed to participate in the Extension Study and complete the questionnaire evaluating parental ages. The number of women who survived to age 90 was thus lower than that who died before age 90. Women who enrolled for additional follow-up in the WHI were more likely to be white, educated, and healthier at baseline. We did not include cognitive status in our definition of healthy aging, because cognitive data were not regularly collected among WHI participants. We also did not have information on birth order. Strengths include a long follow-up period and examination of a diverse cohort of women who survived into advanced ages with information on major chronic diseases and disabilities. There are limited prospective cohorts with information on parental ages and follow-up into late ages to evaluate healthy aging.

Growing numbers of men and women are choosing to postpone parenthood to later ages. Accordingly, understanding the implications of later parental age on the aging of future generations should be a priority for future research. Specifically, it will be important to determine whether parental age is a surrogate for factors such as SES throughout the life course that are associated with aging.

Funding

This work was supported by the National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services [contracts HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C].

The National Heart, Lung, and Blood Institute has representation on the Women's Health Initiative Steering Committee, which governed the design and conduct of the study, the interpretation of the data, and preparation and approval of manuscripts.

Ethics statement

All participants provided written informed consent, and institutional review board approval was received by all participating institutions.

Provenance and peer review

This article has undergone peer review.

Research data (data sharing and collaboration)

There are no linked research data sets for this paper. Individuals who wish to analyze data from the Women's Health Initiative (WHI) are required to have paper proposals approved by the WHI Publications and Presentations Committee.

CRediT authorship contribution statement

Aladdin H. Shadyab: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Validation, Visualization, Writing - original draft, Writing - review & editing. **JoAnn E. Manson:** Investigation, Writing - review & editing. **Wenjun Li:** Methodology, Investigation, Writing - review & editing. **Margery Gass:** Investigation, Writing - review & editing. **Robert L. Brunner:** Investigation, Writing - review & editing. **Michelle J. Naughton:** Investigation, Writing - review & editing. **Brad**

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Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Acknowledgements

We would like to acknowledge the following Women's Health Initiative Investigators:

Program Office: (National Heart, Lung, and Blood Institute, Bethesda, Maryland) Jacques Rossouw, Shari Ludlam, Dale Burwen, Joan McGowan, Leslie Ford, and Nancy Geller.

Clinical Coordinating Center: (Fred Hutchinson Cancer Research Center, Seattle, WA) Garnet Anderson, Ross Prentice, Andrea LaCroix, and Charles Kooperberg.

Investigators and Academic Centers: (Brigham and Women's Hospital, Harvard Medical

School, Boston, MA) JoAnn E. Manson; (MedStar Health Research Institute/Howard University,

Washington, DC) Barbara V. Howard; (Stanford Prevention Research Center, Stanford, CA)

Marcia L. Stefanick; (The Ohio State University, Columbus, OH) Rebecca Jackson; (University

of Arizona, Tucson/Phoenix, AZ) Cynthia A. Thomson; (University at Buffalo, Buffalo, NY)

Jean Wactawski-Wende; (University of Florida, Gainesville/Jacksonville, FL) Marian Limacher;

(University of Iowa, Iowa City/Davenport, IA) Robert Wallace; (University of Pittsburgh,

Pittsburgh, PA) Lewis Kuller; (Wake Forest University School of Medicine, Winston-Salem,NC)

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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.2019.08.002.

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