# Parental longevity predicts healthy ageing among women

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# Abstract

Objective: to examine the association of parental longevity with healthy survival to age 90 years.

**Methods:** this was a prospective study among a racially and ethnically diverse cohort of 22,735 postmenopausal women from the Women's Health Initiative recruited from 1993 to 1998 and followed through 2017. Women reported maternal and paternal ages at death and current age of alive parents. Parental survival categories were <70, 70–79 (reference), 80–89 and  $\geq$ 90 years (longevity). Healthy ageing was defined as reaching age 90 without major chronic conditions (coronary heart disease, stroke, diabetes, cancer, or hip fracture) or physical limitations.

**Results:** women whose mothers survived to  $\geq 90$  years were more likely to attain healthy ageing (OR, 1.25; 95% CI, 1.11–1.42) and less likely to die before age 90 (OR, 0.75; 95% CI, 0.68–0.83). Women whose fathers survived to  $\geq 90$  years did not have significantly increased odds of healthy ageing but showed 21% (OR, 0.79; 95% CI, 0.70–0.90) decreased odds of death before age 90. Women whose mother and father both lived to 90 had the strongest odds of healthy ageing (OR, 1.38; 95% CI, 1.09–1.75) and decreased odds of death (OR, 0.68; 95% CI, 0.54–0.85). The proportion of healthy survivors was highest among women whose mother and father lived to 90 (28.6%), followed by those whose mother only lived to 90 (23.2%).

**Conclusions:** parental longevity predicted healthy ageing in a national cohort of postmenopausal women, supporting the view that genetic, environmental, and behavioral factors transmitted across generations may influence ageing outcomes among offspring.

Keywords: longevity, ageing, healthspan, women, survival, older people

### Introduction

Achieving healthy ageing has become an important public health priority in light of the rapidly growing ageing population in the USA. The traditional definition of healthy ageing encompasses the ability to reach old age with delayed onset of age-related diseases and disabilities [1]. Individuals with exceptional survival often remain healthier for longer periods of time and enjoy better physical function in late life, such that their number of years of survival spent in good health (i.e. healthspan) approaches lifespan [2, 3]. Although genetic, epigenetic, behavioral and lifestyle factors may play a role in this phenomenon [2, 4], factors predicting healthy ageing remain incompletely understood.

Offspring of long-lived parents are more likely to not only live longer, but to also delay onset of age-related diseases (e.g. cardiovascular disease [CVD] and diabetes), have fewer CVD risk factors (e.g. hypertension) and have slower declines in physical and cognitive function [5–20]. In the New England Centenarian Study, offspring of centenarians had 78%, 83% and 86% lower risk of developing myocardial infarction, stroke and diabetes, respectively, than a similarly aged referent cohort [5]. Among Ashkenazi Jewish adults, individuals with either one or two compared with no parents who survived to age 95 had reduced decline in objectively-measured physical function during a median 3-year follow-up period [17].

Few studies have examined parental longevity in relation to a composite measure of healthy ageing that includes both avoidance of major diseases and disability. Previous studies were also limited by small sample sizes and casecontrol designs. A greater understanding of the role of parental longevity in offspring ageing outcomes will shed light on the interplay between demographic, lifestyle and inherited factors allowing some individuals to age successfully. Among the Women's Health Initiative (WHI), we examined associations of maternal and paternal longevity with healthy ageing, defined as survival to age 90 without major chronic conditions (coronary heart disease [CHD], stroke, diabetes, cancer or hip fracture) or physical limitations.

### **Methods**

#### Study population and design

The WHI is a large, prospective study investigating major risk factors for chronic diseases among women. Study details are described in Supplementary Methods, available at *Age and Ageing* online and elsewhere [21]. Women were recruited from 1993 to 1998 and participated in one or more of three clinical trials or an observational study. This study was restricted to participants born on or before 28 February 1927 who had potential, because of birth year, to survive to age 90 during the follow-up period ending 28 February 2017. Only women who had complete information on maternal or paternal survival, survival status and physical function at age 90 were included, leading to an analytic cohort of 22,735 women with up to 22 years of follow-up. All participants provided written informed consent, and institutional review board approval was received by all participating institutions.

#### Parental survival variables

At baseline, women were asked, by questionnaire, whether their natural mother and/or father was still alive. Women who responded affirmatively were asked their natural mother's or father's current age (<70, 70-79, 80-89, 90-99 or  $\geq 100$  years). Women with deceased parents were subsequently asked at what age their biological parents died, selecting from the following categories: <40, 40-49, 50-59, 60-69, 70-79, 80-89, 90-99 or ≥100 years. Parental longevity was defined as having a mother or father who survived to ≥90 years. Maternal and paternal survival variables were categorized as follows: <70, 70-79, 80-89 or ≥90 years. These variables included women whose natural parent died and those whose natural parent was still alive and  $\geq$ 90 years; women whose natural mother or father was still alive but did not reach age 90 were excluded from these variables (n = 121). A third variable representing the number of long-lived parents was created among women with deceased parents, with the following categories: no parent lived to 90; only father lived to 90; only mother lived to 90 and both mother and father lived to 90.

#### **Study variables**

At baseline, participants completed questionnaires assessing age, race/ethnicity, education, income, marital status, diet quality, smoking, alcohol consumption, physical activity, depressive symptoms and self-rated health. Trained clinic staff measured height and weight at baseline. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. Information on history of agerelated diseases (CHD, stroke, cancer, diabetes and hip fracture) was collected at baseline and follow-up (Supplementary Methods, available at *Age and Ageing* online).

#### Study outcome

Participants were classified as having survived to age 90 or died before this age. Trained physician adjudicators confirmed deaths according to 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.

Healthy ageing was defined as survival to  $\geq 90$  years without a history of major age-related diseases and with no limitations in physical function. Although there is no standard definition of healthy ageing, previous definitions were based on Rowe and Kahn's model, which includes avoidance of major diseases and the maintenance of high physical function [1, 22–24]. Late-life physical function status was determined using the physical function subscale of the

RAND 36-item Health Survey collected within 2 years of the 90th birth year and with the least missing data [25]. Values on this scale range from 0 to 100, with higher scores indicating better function. Good physical function was defined as not reporting any of the following limitations, as previously described: limited at least 'a little' on moderate activities (moving a table, vacuuming, bowling, or golfing; climbing one flight of stairs; walking more than one mile; walking several blocks or bathing or dressing) or limited 'a lot' on difficult activities (running, lifting heavy objects or strenuous sports; lifting or carrying groceries; climbing several flights of stairs; or bending, kneeling or stooping) [22]. The outcome variable had three categories, defined similarly to previous studies: healthy survival (survived to age 90 and met the definition of healthy ageing); usual survival (survived to age 90 but did not meet the definition of healthy ageing) and died before age 90 [22-24].

#### Statistical analysis

Comparisons of baseline characteristics by maternal survival, paternal survival and number of long-lived parents were performed using chi-square tests for categorical variables. Normally distributed and non-normally distributed continuous variables were compared by parental survival using analysis of variance and Kruskal–Wallis tests, respectively.

The analytic approach for this study was similar to previous studies examining predictors of ageing outcomes [22-24]. Multinomial logistic regression models were used to examine associations of maternal survival, paternal survival and number of long-lived parents with healthy ageing, with results reported as odds ratios (OR) and 95% confidence intervals (CI). Separate models were fit for each parental survival variable. The reference category for parental survival variables was 70-79 years, because this age range includes the current average age at death, 78.8 years, in the USA [26]. Usual survivors were considered the reference category for the outcome in the analyses. Multivariable models were adjusted for potential confounders including baseline age, WHI study membership (clinical trial or observational study), race/ethnicity, education, marital status, smoking, alcohol consumption, physical activity, diet quality, depressive symptoms, self-rated health and BMI, variables associated with longevity and healthy ageing [22-24]. Tests for linear trend were performed by including parental survival variables as continuous predictors in the models.

In sensitivity analyses, to check for potential bias due to missing late-life functional data, women who survived to age 90 but had missing information on physical function were assumed to have physical limitations at this age in the models. To test the robustness of our definition of healthy ageing, alternative definitions were considered using different classifications for physical limitation. First, physical function was categorized according to the median, with good function indicated by a total score >45. Second, rather than including all domains of function, only mobility was examined; women who reported that their health limited 'a lot' or 'a little' their ability to walk one block or climb one flight of stairs were classified as having mobility disability.

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

#### Results

Women were aged 73.5 (standard deviation 2.6; range, 68–81) years on average at baseline. Among the overall cohort, 19.0% experienced healthy survival to age 90, 27.6% had usual survival to age 90, and 53.5% died before age 90.

At baseline, women whose mothers lived longer were more likely to be white, college graduates, married or living as married, and current drinkers, and have excellent self-rated health, higher incomes and higher diet quality (Table 1). They were less likely to be obese, have depressive symptoms, or experience age-related diseases including CHD, stroke or diabetes. Similar differences were observed when comparing women according to paternal survival and number of longlived parents (Table 2 and Supplementary Table 1, available at *Age and Ageing* online).

Compared with women whose mothers lived to 70–79 years, women whose mothers lived to  $\geq 90$  years had 25% (OR, 1.25; 95% CI, 1.11–1.42) increased odds of survival to age 90 without major diseases or physical limitations (Table 3). Women whose mothers lived to  $\geq 90$  years had 25% (OR, 0.75; 95% CI, 0.68–0.83) decreased odds of death before age 90. Compared with women whose fathers lived to 70–79 years, women whose fathers achieved longevity did not have increased odds of healthy ageing (OR, 1.11; 95% CI, 0.96–1.29) but had 21% (OR, 0.79; 95% CI, 0.70–0.90) decreased odds of death before age 90. Increasing maternal and paternal survival were significantly linearly associated with healthy ageing (*P*-values for trend = 0.008 and 0.006, respectively) and death before age 90 (*P*-values for trend = 0.001 and 0.008, respectively).

Compared with women without any long-lived parents, women with only long-lived mothers had increased odds of healthy ageing (OR, 1.19; 95% CI, 1.06–1.32), whereas women with only long-lived fathers did not have increased odds of healthy ageing (OR, 1.12; 95% CI, 0.95–1.32) (Table 3). Women with a single long-lived parent had similar decreased odds of death before age 90 (Table 3). The strongest odds of healthy ageing were among women whose mother and father both lived to 90 (OR, 1.38; 95% CI, 1.09–1.75); these women were also the least likely to die before age 90 (OR, 0.68; 95% CI, 0.54–0.85). Women with two long-lived parents had the highest proportion of healthy survivors (28.6%), and women with no long-lived parent had the highest proportion of death before age 90 (56.2%) (Supplementary Figure 1, available at *Age and Ageing* online).

In sensitivity analyses assuming that women with missing data on physical function had physical limitations at age 90, findings in multivariable models were similar. In analyses using

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Table I. Baseline characteristics of postmenopausal	women from the	Women's Health Initiativ	e by maternal survival,
1993–1998 ( $N = 22,548$ ) <sup>a</sup>			

	Maternal survival, years				P-value
	<70 (N = 5,747)	70–79 (N = 4,636)	80–89 (N = 6,942)	$\geq 90$ (N = 5,223)	
Age, mean (SD), years	73.7 (2.6)	73.5 (2.5)	73.4 (2.6)	73.5 (2.5)	< 0.001
Race/ethnicity	15.1 (2.0)	15.5 (2.5)	75.4 (2.0)	15.5 (2.5)	<0.001
White	4,965 (86.7)	4,177 (90.5)	6,388 (92.3)	4,768 (91.6)	
Black	449 (7.8)	243 (5.3)	284 (4.1)	181 (3.5)	< 0.001
Hispanic	98 (1.7)	50 (1.1)	74 (1.1)	73 (1.4)	-0.001
Other	214 (3.7)	144 (3.1)	178 (2.6)	183 (3.5)	
Educational level	211 (0.7)	111 (011)	1/0 (210)	100 (010)	
Less than high school	465 (8.1)	302 (6.6)	355 (5.1)	209 (4.0)	
High school	1,105 (19.3)	853 (18.5)	1,202 (17.4)	831 (16.0)	< 0.001
Some college	2,292 (40.1)	1,763 (38.3)	2,749 (39.8)	2,070 (39.8)	-0.001
College graduate	1,853 (32.4)	1,688 (36.7)	2,598 (37.6)	2,089 (40.2)	
Income	-,	-,	_,	_,,	
<\$20,000	1,607 (30.3)	1,196 (27.7)	1,555 (24.1)	1,011 (21.0)	
\$20,000-<\$50,000	2,632 (49.6)	2,146 (49.7)	3,389 (52.4)	2,494 (51.9)	< 0.001
≥\$50,000	1,070 (20.2)	975 (22.6)	1,523 (23.6)	1,304 (27.1)	-0.001
Marital status	-,••• (=••=)	,	-,	-,	
Married/living as married	2,679 (46.8)	2,214 (47.9)	3,463 (50.1)	2,723 (52.3)	
Widowed	2,205 (38.5)	1,697 (36.8)	2,473 (35.8)	1,742 (33.5)	< 0.001
Divorced/separated	606 (10.6)	475 (10.3)	697 (10.1)	517 (9.9)	-0.001
Never married	236 (4.1)	232 (5.0)	282 (4.1)	225 (4.3)	
Smoking behavior	200 (11)	202 (010)	202 (111)	220 (110)	
Never smoked	3,098 (54.9)	2,481 (54.4)	3,690 (53.9)	2,834 (55.0)	
Past smoker	2,263 (40.1)	1,899 (41.7)	2,855 (41.7)	2,102 (40.8)	0.09
Current smoker	285 (5.1)	179 (3.9)	301 (4.4)	221 (4.3)	0.07
Alcohol intake				()	
Nondrinker	785 (13.8)	577 (12.6)	822 (11.9)	618 (11.9)	
Past drinker	1,274 (22.4)	1,010 (22.0)	1,341 (19.4)	929 (17.9)	< 0.001
Current drinker	3,628 (63.8)	3,010 (65.5)	4,737 (68.7)	3,642 (70.2)	-0.001
Recreational physical activity, mean (SD), MET-hours/week	12.0 (12.9)	12.0 (13.5)	12.3 (13.1)	12.5 (12.8)	0.001
Healthy eating index score, mean (SD)	68.8 (10.6)	68.9 (10.3)	69.4 (10.2)	69.2 (10.3)	0.01
Body mass index, $kg/m^2$	0010 (1010)	0010 (1015)	0,11 (1012)	0)12 (1010)	0.01
Underweight	81 (1.4)	54 (1.2)	64 (0.9)	81 (1.6)	
Normal weight	2,006 (35.2)	1,704 (37.2)	2,597 (37.8)	2,063 (39.8)	< 0.001
Overweight	2,086 (36.6)	1,673 (36.5)	2,545 (37.0)	1,941 (37.4)	
Obese	1,521 (26.7)	1,156 (25.2)	1,669 (24.3)	1,100 (21.2)	
Burnham depression scale score $\geq 0.06$	488 (8.8)	406 (9.0)	533 (7.9)	363 (7.2)	0.002
History of major age-related diseases					
Coronary heart disease	1,030 (17.9)	776 (16.7)	977 (14.1)	595 (11.4)	< 0.001
Stroke	748 (13.0)	574 (12.4)	792 (11.4)	516 (9.9)	< 0.001
Cancer	1,802 (31.4)	1,455 (31.4)	2,219 (32.0)	1,607 (30.8)	0.57
Diabetes	958 (16.7)	775 (16.7)	1,017 (14.7)	680 (13.0)	< 0.001
Hip fracture	428 (7.5)	339 (7.3)	507 (7.3)	376 (7.2)	0.97
≥1 Disease	3,557 (61.9)	2,846 (61.4)	4,090 (58.9)	2,889 (55.3)	< 0.001
Self-rated health	-, (010)	_, (0111)	., (000)	_,	-0.001
Excellent	644 (11.3)	526 (11.4)	936 (13.6)	797 (15.3)	
Very good	2,120 (37.3)	1,750 (38.0)	2,768 (40.2)	2,215 (42.6)	< 0.001
Good	2,208 (38.8)	1,802 (39.2)	2,499 (36.3)	1,739 (33.5)	-0.001
Fair/poor	717 (12.6)	525 (11.4)	688 (10.0)	447 (8.6)	

MET, metabolic equivalent; SD, standard deviation.

<sup>a</sup>Values are represented as No. (%), unless otherwise indicated. Data do not sum to total due to missing data.

alternative classifications for physical limitation in definitions of healthy ageing, findings were similar (data not shown).

# Discussion

Among a national cohort of >22,000 postmenopausal women, parental longevity predicted survival to age 90 free

of major age-related diseases and physical limitations. Women whose mothers survived to  $\geq 90$  years had 25% increased likelihood of achieving healthy ageing. Having both a mother and father who achieved longevity was associated with the strongest likelihood of healthy ageing. These findings support the notion that individuals with familial longevity may be more likely to not only achieve longevity

### Parental longevity predicts healthy ageing among women

	Paternal survival, years				P-value
	<70 (N = 8,552)	70–79 (N = 6,124)	80–89 (N = 5,434)	≥90 (N = 2,181)	
Age, mean (SD), years	73.5 (2.6)	73.5 (2.6)	73.5 (2.6)	73.5 (2.5)	0.59
Race/ethnicity	(515 (210)	(210)	(515 (210)	(515 (215)	0.07
White	7,641 (89.7)	5,572 (91.3)	4,941 (91.3)	1,942 (89.2)	
Black	504 (5.9)	289 (4.7)	233 (4.3)	88 (4.0)	< 0.001
Hispanic	123 (1.4)	59 (0.9)	65 (1.2)	40 (1.8)	.01001
Other	253 (3.0)	182 (3.0)	174 (3.2)	108 (5.0)	
Educational level		()			
Less than high school	585 (6.9)	358 (5.9)	261 (4.8)	100 (4.6)	
High school	1,582 (18.6)	1,101 (18.1)	934 (17.3)	310 (14.3)	< 0.001
Some college	3,482 (41.0)	2,357 (38.7)	2,102 (38.8)	829 (38.1)	
College graduate	2,849 (33.5)	2,271 (37.3)	2,116 (39.1)	935 (43.0)	
Income	, , , ,	, , ,	, , , ,	· · · ·	
<\$20,000	2,189 (27.6)	1,486 (26.2)	1,207 (23.9)	414 (20.5)	
\$20,000-<\$50,000	3,976 (50.2)	2,887 (50.9)	2,630 (52.1)	1,046 (51.9)	< 0.001
≥\$50,000	1,760 (22.2)	1,294 (22.8)	1,216 (24.1)	556 (27.6)	
Marital status		· · · · ·	· · · · ·		
Married/living as married	4,102 (48.1)	3,003 (49.2)	2,747 (50.8)	1,129 (51.9)	
Widowed	3,165 (37.1)	2,180 (35.7)	1,911 (35.3)	759 (34.9)	0.01
Divorced/separated	891 (10.5)	632 (10.4)	533 (9.9)	187 (8.6)	
Never married	364 (4.3)	284 (4.7)	221 (4.1)	100 (4.6)	
Smoking behavior		. ,	. ,	. ,	
Never smoked	4,508 (53.4)	3,213 (53.4)	3,019 (56.4)	1,232 (57.4)	
Past smoker	3,520 (41.7)	2,527 (42.0)	2,131 (39.8)	832 (38.8)	< 0.001
Current smoker	407 (4.8)	283 (4.7)	203 (3.8)	82 (3.8)	
Alcohol intake					
Nondrinker	1,005 (11.9)	701 (11.5)	758 (14.0)	297 (13.7)	
Past drinker	1,811 (21.4)	1,285 (21.2)	1,030 (19.1)	386 (17.8)	< 0.001
Current drinker	5,661 (66.8)	4,090 (67.3)	3,612 (66.9)	1,487 (68.5)	
Recreational physical activity, mean (SD), MET-hours/week	11.8 (12.9)	12.4 (13.3)	12.5 (13.4)	12.3 (12.3)	0.001
Healthy eating index score, mean (SD)	68.8 (10.4)	69.2 (10.3)	69.3 (10.4)	69.6 (10.2)	0.005
Body mass index, $kg/m^2$					
Underweight	103 (1.2)	84 (1.4)	55 (1.0)	37 (1.7)	
Normal weight	3,061 (36.1)	2,288 (37.7)	2,102 (39.1)	824 (38.0)	0.002
Overweight	3,151 (37.2)	2,234 (36.9)	1,968 (36.6)	823 (38.0)	
Obese	2,161 (25.5)	1,457 (24.0)	1,256 (23.3)	482 (22.3)	
Burnham depression scale score ≥0.06	716 (8.7)	483 (8.1)	410 (7.7)	156 (7.4)	0.12
History of major age-related diseases					
Coronary heart disease	1,458 (17.1)	918 (15.0)	702 (12.9)	261 (12.0)	< 0.001
Stroke	1,031 (12.1)	684 (11.2)	645 (11.9)	230 (10.6)	0.13
Cancer	2,697 (31.5)	1,933 (31.6)	1,699 (31.3)	679 (31.1)	0.97
Diabetes	1,407 (16.5)	900 (14.7)	785 (14.5)	302 (13.9)	< 0.001
Hip fracture	562 (6.6)	486 (7.9)	423 (7.8)	158 (7.2)	0.007
≥1 Disease	5,200 (60.8)	3,625 (59.2)	3,156 (58.1)	1,242 (57.0)	< 0.001
Self-rated health					
Excellent	991 (11.7)	792 (13.0)	753 (14.0)	336 (15.5)	
Very good	3,247 (38.3)	2,362 (38.8)	2,234 (41.4)	931 (43.0)	< 0.001
Good	3,262 (38.4)	2,249 (37.0)	1,906 (35.3)	731 (33.8)	
Fair/poor	987 (11.6)	679 (11.2)	503 (9.3)	165 (7.6)	

**Table 2.** Baseline characteristics of postmenopausal women from the Women's Health Initiative by paternal survival,  $1993-1998 (N = 22,291)^{a}$ 

MET, metabolic equivalent; SD, standard deviation.

<sup>a</sup>Values are represented as No. (%), unless otherwise indicated. Data do not sum to total due to missing data.

themselves but to also enjoy their later years without morbidity or disability.

Our findings agree with prior studies showing that offspring of long-lived parents may live longer and healthier lives [5–20]. A study among Italians observed that, compared with an age-matched group without long-lived parents and from a similar birth cohort, offspring of centenarians had lower BMI and smaller proportion of obese individuals, and were also more likely to be able to walk 500 meters without requiring help [20]. In a recent study among >186,000 participants, increasing parental survival was associated with greater education, higher income, more physical activity, less smoking and lower prevalence of obesity, similar to our study [6]. We found that parental longevity predicted

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	Healthy survival to age 90 vs. usual survival to age $90^{a}$		Death before age 90 vs. usual survival to age 90		
	Crude <sup>b</sup> O	Multivariable-adjusted <sup>c,d</sup> R (95% CI)	Crude <sup>b</sup> Ol	Multivariable-adjusted <sup>c,d</sup> R (95% CI)	
Maternal survival, years				·····	
<70	1.02 (0.90-1.15)	1.05 (0.92-1.20)	0.98 (0.89-1.07)	0.95 (0.86-1.05)	
70–79	1.00 [ref]	1.00 [ref]	1.00 [ref]	1.00 [ref]	
80-89	1.12 (0.99–1.25)	1.08 (0.96–1.23)	0.94 (0.86–1.02)	0.95 (0.86–1.04)	
≥90	1.29 (1.15-1.45)	1.25 (1.11–1.42)	0.72 (0.65-0.79)	0.75 (0.68–0.83)	
Paternal survival, years		× ,	( )		
<70	0.89 (0.81-0.99)	0.90 (0.81-1.00)	1.02 (0.95-1.11)	1.00 (0.92-1.09)	
70–79	1.00 [ref]	1.00 [ref]	1.00 [ref]	1.00 [ref]	
80-89	1.01 (0.90-1.12)	0.98 (0.87–1.10)	0.93 (0.86-1.02)	0.96 (0.87–1.06)	
≥90	1.12 (0.98-1.29)	1.11 (0.96–1.29)	0.74 (0.66-0.83)	0.79 (0.70-0.90)	
Number of long-lived parents					
No parent lived to 90	1.00 [ref]	1.00 [ref]	1.00 [ref]	1.00 [ref]	
Only father lived to 90	1.12 (0.96-1.31)	1.12 (0.95–1.32)	0.75 (0.66-0.85)	0.80 (0.70-0.92)	
Only mother lived to 90	1.20 (1.09-1.33)	1.19 (1.06–1.32)	0.75 (0.69-0.81)	0.80 (0.73-0.87)	
Both mother and father lived to 90	1.45 (1.16-1.81)	1.38 (1.09–1.75)	0.64 (0.52-0.79)	0.68 (0.54-0.85)	

 Table 3. Multivariable associations of parental longevity with healthy survival to age 90 among postmenopausal women from the Women's Health Initiative, 1993–2017

CI, confidence interval; OR, odds ratio.

<sup>a</sup>Healthy survival defined as: survival to age 90 free of major chronic diseases (coronary heart disease, stroke, cancer, diabetes or hip fracture) and physical limitations.

<sup>b</sup>Crude model adjusted for age and race/ethnicity.

<sup>c</sup>Multivariable model adjusted for age, race/ethnicity, study component (observational study or clinical trial), education, marital status, smoking, alcohol consumption, diet quality, body mass index, depressive symptoms, physical activity and self-rated health.

<sup>d</sup>Maternal longevity: *P-value for trend* = 0.008 (healthy survival) and 0.001 (death); paternal longevity: *P-value for trend* = 0.006 (healthy survival) and 0.008 (death).

healthy ageing after adjustment for these confounders, suggesting that sociodemographic and lifestyle factors do not entirely explain associations of parental longevity with healthy ageing.

Parental longevity likely represents the combined effects of genetic, behavioral and environmental factors transmitted across generations that, throughout the life course, influence ageing outcomes among offspring. The protective association between parental longevity and adverse health outcomes may be largely due to genetic factors [4, 27, 28]. In a recent genome-wide association study, 10 genetic loci were associated with attained parental age, including APOE, a gene associated with longevity [4, 27, 28]. In the WHI, single nucleotide polymorphisms representing variation in APOE were associated with longevity and a composite outcome of healthy ageing defined similarly to the one used in the present study [27]. Offspring may inherit genetic factors that protect against major diseases and disability; however, it is unknown whether a similar set of genetic factors influences both disease and disability.

The ability to maintain physical function in old age is a key component of healthy ageing [1]. Parental longevity has been linked to less decline in physical function in ageing [17, 18]. Besides environmental factors, variation in late-life disability is also partly attributable to genetic factors [29, 30], a finding that is supported by the association of parental longevity with survival to age 90 without physical limitations in the present study. Variation in *APOE* has been associated with increased risk of gait speed decline and disability among community-dwelling older adults and was associated with disability-free survival in the WHI [27, 30].

Our study has several limitations. Women who consented to further follow-up were more likely to be white, educated, and healthier at baseline than those who were lost to follow-up, thus findings may be biased by selective attrition. Parental age at death was based upon participant report and not validated, which may have resulted in misclassification. Women whose natural mother or father was still alive but did not reach age 90 were not included; however, as reported, a small number of women met this criterion. We did not evaluate cognitive outcomes, such as dementia, in our definition of healthy ageing, due to limited data because they were not collected regularly among all WHI participants. Finally, we lacked information on parental cause of death.

Strengths of our study include the ethnically diverse cohort, large sample size and 22 years of follow-up with information on late-life physical function. Our study examined a large number of women who survived to age 90 and who achieved healthy ageing as defined by this study. We were able to examine both paternal and maternal survival and had information on many confounders and adjudicated chronic diseases. Finally, any confounding due to birth cohort effects was minimized due to the narrow baseline age range of the cohort.

In summary, maternal and paternal longevity predicted survival to age 90 without major chronic conditions or physical limitations in a national cohort of postmenopausal women. Our findings suggest that daughters of long-lived parents may be more likely to live a long and healthy life. From a public health perspective, future studies with life course data are needed to clarify how environmental factors and behaviors, some of which are transmitted across generations, interact with genetic and epigenetic factors to influence ageing outcomes.

# **Key points**

- We examined the association between parental longevity and healthy ageing to 90 years among women.
- Women whose mother and father both lived to 90 had the greatest chances of achieving healthy ageing.
- Examined separately, maternal, but not paternal, longevity was associated with increased likelihood of healthy ageing.
- Daughters of long-lived parents may be more likely to live a long and healthy life.
- Genetic, environmental and behavioral factors transmitted across generations may influence ageing outcomes among offspring.

# Supplementary Data

Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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# **Ethics Approval**

Fred Hutchinson Cancer Research Center Ethics Committee, Seattle, WA.

# **Conflicts of interest**

None.

# References

- 1. Rowe JW, Kahn RL. Successful aging. Gerontologist 1997; 37: 433–40.
- **2.** Newman AB, Murabito JM. The epidemiology of longevity and exceptional survival. Epidemiol Rev 2013; 35: 181–97.
- Ismail K, Nussbaum L, Sebastiani P et al. Compression of morbidity is observed across cohorts with exceptional longevity. J Am Geriatr Soc 2016; 64: 1583–91.
- Shadyab AH, LaCroix AZ. Genetic factors associated with longevity: a review of recent findings. Ageing Res Rev 2015; 19: 1–7.
- 5. Adams ER, Nolan VG, Andersen SL, Perls TT, Terry DF. Centenarian offspring: start healthier and stay healthier. J Am Geriatr Soc 2008; 56: 2089–92.
- 6. Atkins JL, Pilling LC, Ble A *et al.* Longer-lived parents and cardiovascular outcomes: 8-year follow-up in 186,000 U.K. Biobank participants. J Am Coll Cardiol 2016; 68: 874–5.
- Dutta A, Henley W, Robine JM, Langa KM, Wallace RB, Melzer D. Longer lived parents: protective associations with cancer incidence and overall mortality. J Gerontol A Biol Sci Med Sci 2013; 68: 1409–18.
- Gubbi S, Schwartz E, Crandall J *et al.* Effect of exceptional parental longevity and lifestyle factors on prevalence of cardiovascular disease in offspring. Am J Cardiol 2017; 120: 2170–5.
- **9.** Yarnell J, Yu S, Patterson C *et al.* Family history, longevity, and risk of coronary heart disease: the PRIME Study. Int J Epidemiol 2003; 32: 71–7.
- Terry DF, Wilcox MA, McCormick MA, Perls TT. Cardiovascular disease delay in centenarian offspring. J Gerontol A Biol Sci Med Sci 2004; 59: 385–9.
- **11.** Ikeda A, Iso H, Toyoshima H *et al.* Parental longevity and mortality amongst Japanese men and women: the JACC study. J Intern Med 2006; 259: 285–95.
- 12. Reed T, Carmelli D, Robinson TS, Rinehart SA, Williams CJ. More favorable midlife cardiovascular risk factor levels in male twins and mortality after 25 years of follow-up is related to longevity of their parents. J Gerontol A Biol Sci Med Sci 2003; 58: 367–72.

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- **13.** Barzilai N, Gabriely I, Gabriely M, Iankowitz N, Sorkin JD. Offspring of centenarians have a favorable lipid profile. J Am Geriatr Soc 2001; 49: 76–9.
- 14. Terry DF, Evans JC, Pencina MJ *et al.* Characteristics of Framingham offspring participants with long-lived parents. Arch Intern Med 2007; 167: 438–44.
- Shavelle R, Paculdo D. The effect of exceptional parental longevity on life expectancy. J Am Geriatr Soc 2012; 60: 1185.
- Terry DF, Wilcox MA, McCormick MA *et al.* Lower allcause, cardiovascular, and cancer mortality in centenarians' offspring. J Am Geriatr Soc 2004; 52: 2074–6.
- 17. Ayers E, Barzilai N, Crandall JP, Milman S, Verghese J. Association of family history of exceptional longevity with decline in physical function in aging. J Gerontol A Biol Sci Med Sci 2017; 72: 1649–55.
- Ayers E, Barzilazi N, Crandall JP, Milman S, Verghese J. Association of exceptional parental longevity and physical function in aging. Age 2014; 36: 9677.
- **19.** Lipton RB, Hirsch J, Katz MJ *et al.* Exceptional parental longevity associated with lower risk of Alzheimer's disease and memory decline. J Am Geriatr Soc 2010; 58: 1043–9.
- 20. Bucci L, Ostsan R, Cevenini E *et al.* Centenarians' offspring as a model of healthy aging: a reappraisal of the data on Italian subjects and a comprehensive overview. Aging 2016; 8: 510–19.
- **21.** The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. Control Clin Trials 1998; 19: 61–109.
- 22. Sun Q, Townsend MK, Okereke OI, Franco OH, Hu FB, Grodstein F. Adiposity and weight change in mid-life in

relation to healthy survival after age 70 in women: prospective cohort study. BMJ 2009; 339: b3796.

- **23.** Rillamas-Sun E, LaCroix AZ, Waring ME *et al.* Obesity and late-age survival without major disease or disability in older women. JAMA Intern Med 2014; 174: 98–106.
- 24. Willcox BJ, He Q, Chen R *et al.* Midlife risk factors and healthy survival in men. JAMA 2006; 296: 2343–50.
- **25.** Hays RD, Sherbourne CD, Mazel RM. The RAND 36-item health survey, 1.0. Health Econ 1993; 2: 217–27.
- **26.** Centers for Disease Control and Prevention. Life expectancy. Available at https://www.cdc.gov/nchs/fastats/life-expectancy. htm. Accessed December 10, 2017.
- 27. Shadyab AH, Kooperberg C, Reiner AP *et al.* Replication of genome-wide association study findings of longevity in white, African American, and Hispanic women: The Women's Health Initiative. J Gerontol A Biol Sci Med Sci 2017; 72: 1401–6.
- **28.** Pilling LC, Kuo CL, Sicinski K *et al.* Human longevity: 25 genetic loci associated in 389,166 UK biobank participants. Aging 2017; 9: 2504–20.
- **29.** Kulminski A, Ukraintseva SV, Arbeev KG *et al.* Association between APOE epsilon 2/epsilon 3/epsilon 4 polymorphism and disability severity in a national long-term care survey sample. Age Ageing 2008; 37: 288–93.
- 30. Verghese J, Holtzer R, Wang C, Katz MJ, Barzilai N, Lipton RB. Role of APOE genotype in gait decline and disability in aging. J Gerontol A Biol Sci Med Sci 2013; 68: 1395–1401.

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# Happy older people live longer

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# Abstract

**Objective:** research on the role of positive affect, such as happiness, on health outcomes is burgeoning. Within this context, evidence for an inverse effect of happiness on mortality is inconclusive. Furthermore, few studies link happiness with mortality among older people, and in Asian populations. We examine the association between happiness and all-cause mortality among older people in Singapore.

**Methods:** data for 4,478 Singaporeans aged  $\geq 60$  years enrolled in a nationally-representative longitudinal survey (three waves: 2009; 2011; 2015) were utilised. Happiness, at baseline, in 2009, was measured using three positively-worded items from the Centre for Epidemiological Studies Depression Scale, and considered in two distinct ways in the analyses—continuous ('happiness score' [0–6]) and binary (happy [score = 6]/unhappy). All-cause mortality, until 31 December 2015, was