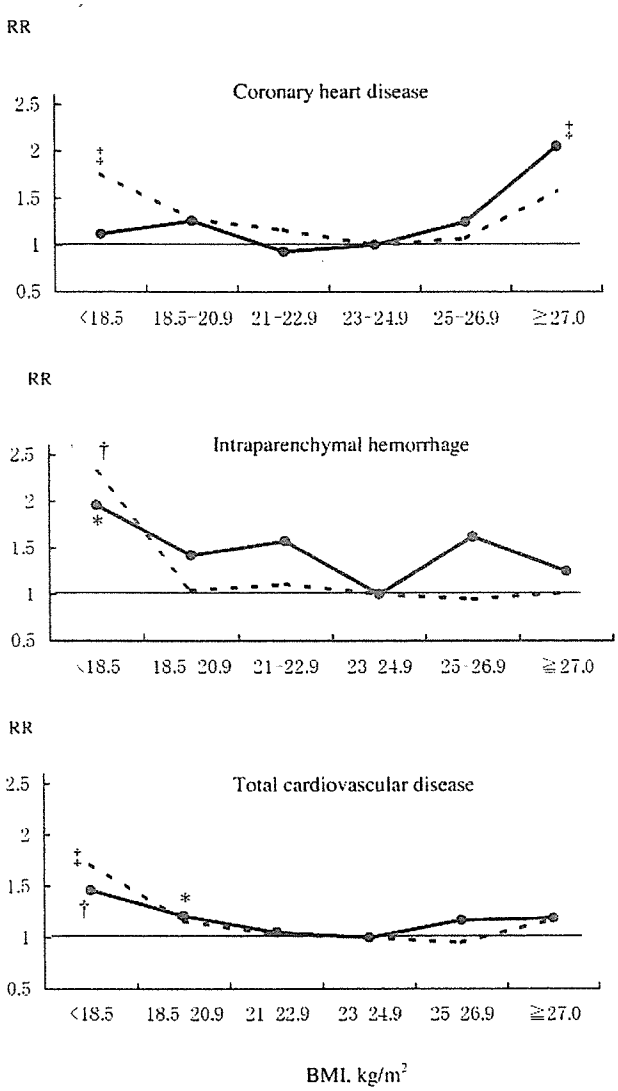

Sex-specific multivariate relative risks (RR) of mortality from coronary heart disease, intraparenchymal hemorrhage, and total cardiovascular disease according to BMI. Solid line represents men; dotted line, women. Reference group was persons with BMI of 23.0 to 24.9 kg/m^2. Test for significance *P<0.05; †P<0.01; ‡P<0.001.

cardiovascular deaths attributable to individuals with BMI ≥30 kg/m^2.[1] We did not examine the effect of BMI ≥30.0 kg/m^2 because only 1.6% of the participants (1.0% men and 2.0% women) had this high BMI category. According to the 1998 National Nutrition Survey of Japan, the prevalence of persons with BMI ≥30.0 kg/m^2 had 2.5% for men and 3.6% for women aged ≥15 years.[8] This prevalence was much lower than that in the United States (17.7% for men and 18.1% for women in 1998).[2]

The excess risk of intraparenchymal hemorrhage among men with BMI <18.0 kg/m^2 has been reported recently in Korean men,[11] which was consistent with our results. However, in that study, there was also an excess risk from intraparenchymal hemorrhage among overweight men, showing a U-shaped association with BMI. The Physicians' Health Study suggested an excess risk of fatal hemorrhagic stroke among US white men with BMI <23.0 kg/m^2.[12] The Nurses' Health Study showed that the excess risk of hemorrhagic stroke among US women with BMI <21.0 kg/m^2 was confined to smokers.[4] However, our study showed that the excess risk of mortality from intraparenchymal hemorrhage was similarly observed for smokers and nonsmokers. The excess risk of hemorrhagic stroke among Asians with BMI <18.0 to 18.5 kg/m^2 and among Americans with BMI <21.0 to 23.0 kg/m^2 suggests that low BMI, the cut points of which are different among ethnicities, may be a marker for increased risk of hemorrhagic stroke and not so much causally associated.

Associations between low serum total cholesterol and risk of intraparenchymal hemorrhage in previous prospective studies[15,16] and a positive correlation between cholesterol and BMI in the present study suggest low cholesterol as part of a potential causal pathway between low BMI and intraparenchymal hemorrhage. It is also possible that low cholesterol may be a marker for something else that increased the risk of intraparenchymal hemorrhage.

The present study has several limitations. We used self-reported weight and height at enrollment to calculate BMI, in which measurement error may exist: an underestimation of weight and an overestimation of height.[17] However, a previous study of 1823 men and women aged 40 to 68 years showed that BMI estimated from self-reporting was highly correlated with actual BMI (r=0.94), and their mean difference was small (mean±SD=23.3±3.0 versus 23.2±2.9).[18] Second, we used the mortality data, not incident data, as end points, which may lead to misclassification in the diagnosis of stroke subtypes in particular. However, a widespread use of computed tomography scans in Japanese local hospitals since the 1980s has probably made a death certificate diagnosis of stroke subtypes sufficiently accurate.[19]

In conclusion, high BMI was associated with increased risk of mortality from coronary heart disease, whereas low BMI was associated with intraparenchymal hemorrhage, showing a U-shaped relationship between BMI and total cardiovascular disease for Japanese men and women.

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(2) 健診への関心・受診状況とその後の死亡リスク

目的：健診を受診しても、健診への関心が低くその後の保健指導に結びつかない人の健康影響は明らかでない。そこで健診への関心と受診状況がその後の死亡に与える影響について、コホート研究により明らかにすることを目的とした。

方法：文部科学省大規模コホートの対象者に対し、1989 年から 1990 年に質問紙により調査を行い、健診に対する関心と最近 1 年間での健診受診の有無の質問に回答した 68,825 人について、健診への関心・受診の有無と死亡の関連を分析した。年齢、Body Mass Index 等を調整した相対危険度を算出した。

結果：関心がありかつ受診している」に対して「関心がないが受診している」群での相対危険度(95%CI)は、男の循環器疾患では 1.4(1.0-1.8)、全死亡では 1.2 (1.1-1.4)、女ではそれぞれ 1.3(0.9-1.8)、1.3(1.1-1.5)であった。また、「関心がありかつ受診している」に対して「関心がなく未受診である」群での相対危険度は、男の循環器疾患では 1.4(1.1-1.6)、全死亡では 1.2(1.1-1.4)，女ではそれぞれ 1.5(1.2-1.8)、1.4(1.2-1.7)であった。がん死亡に関しては、上記の関連は男女とも認められなかった。

考察：循環器疾患の予防のためには、男では健診に関心がなく受診していない群と健診への関心がないが受診している群、女では健診に関心がなく受診していない群に対して、特に健康教育の必要性が示された。

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The relationships between interest for and participation in health screening and risk of mortality: The Japan Collaborative Cohort Study

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Abstract

Background. This study examined whether the interest in participation in health screening is associated with reduced mortality in Japan.

Methods. A total of 68,825 subjects, 40–79 years old, in 29 Japanese communities responded to a questionnaire including interest level and participation status in health screening during 1988–1990. Systematic surveillance was completed until the end of 1999, with 660,682 person–years of follow-up, and the causes of death were determined.

Results. Men and women with low/no interest in health screening had 24–94% higher mortality from cardiovascular disease (CVD) and all causes. Women, but not men, with non-participation in health screening had 18–24% excess risk of mortality from cardiovascular disease, cancer, and all causes. Men and women with low/no interest and non-participation in health screening had 23–47% excess risk of mortality from cardiovascular disease and all causes. A similar excess risk of mortality was found among men with low/no interest and participation in health screening, but such a trend was less evident among women.

Conclusion. Men and women with lower interest and women with no participation in health screening were at high risk for cardiovascular disease and all-cause mortality. Additionally, men who participated but had lower interest in health screening are also considered as high risk for cardiovascular disease.

Keywords: Health screening; Interest; Mortality; Cohort study

Introduction

In Japan, there are nationwide health promotion programs, including health screening and educational programs (Ishikawa and Seo, 1999). An intervention study has shown benefits of participation in health promotion activities, including positive changes in awareness of risk factors

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Table 1
Sex-specific, age-adjusted and multivariate relative risks and 95% confidence intervals of mortality from total cardiovascular disease, total cancer, and all causes according to the degree of interest and participation in screening

	Degree of interest					Participation in screening	
	High Interest	Moderate +Interest	Low Interest	No Interest	*P* value for Trend	Yes	No
Men							
Total cardiovascular disease							
Person–years	70,868	149,634	44,170	5579		130,043	140,407
Number of cases	274	520	177	41		424	588
Incident rate (per 1000 person–years)	3.87	3.48	4.01	7.35		3.26	4.19
Age-adjusted RR (95% CI)	1.0	1.01 (0.87, 1.17)	1.29 (1.07, 1.56)	1.97 (1.42, 2.73)	<0.001	1.0	1.09 (0.96, 1.23)
Multivariate RR (95% CI)[a]	1.0	1.05 (0.91, 1.22)	1.29 (1.06, 1.56)	1.94 (1.38, 2.72)	<0.001	1.0	1.05 (0.92, 1.19)
Multivariate RR (95% CI)[b]	1.0	1.05 (0.91, 1.22)	1.29 (1.06, 1.57)	1.94 (1.38, 2.72)	<0.001	1.0	1.00 (0.88, 1.14)
Total cancer							
Person–years	70,887	149,695	44,211	5796		151,821	118,769
Number of cases	393	810	237	44		790	694
Incident rate (per 1000 person–years)	5.54	5.41	5.36	7.63		5.20	5.84
Age-adjusted RR (95% CI)	1.0	1.09 (0.97, 1.23)	1.19 (1.01, 1.40)	1.49 (1.09, 2.03)	0.08	1.0	1.09 (0.98, 1.21)
Multivariate RR (95% CI)[a]	1.0	1.08 (0.95, 1.22)	1.13 (0.96, 1.33)	1.35 (0.98, 1.85)	0.33	1.0	1.08 (0.97, 1.20)
Multivariate RR (95% CI)[b]	1.0	1.08 (0.95, 1.22)	1.12 (0.95, 1.32)	1.32 (0.96, 1.82)	0.40	1.0	1.06 (0.96, 1.18)
All causes							
Person–years	70,868	149,634	44,170	5779		184,843	85,607
Number of cases	971	1942	635	128		2408	1268
Incident rate (per 1000 person–years)	13.7	13.0	14.4	22.1		13.0	14.8
Age-adjusted RR (95% CI)	1.0	1.06 (0.98, 1.14)	1.29 (1.17, 1.42)	1.74 (1.45, 2.10)	<0.001	1.0	1.07 (1.00, 1.15)
Multivariate RR (95% CI)[a]	1.0	1.06 (0.98, 1.15)	1.24 (1.12, 1.37)	1.58 (1.31, 1.91)	<0.001	1.0	1.04 (0.96, 1.11)
Multivariate RR (95% CI)[b]	1.0	1.06 (0.98, 1.15)	1.24 (1.12, 1.37)	1.58 (1.31, 1.91)	<0.001	1.0	1.00 (0.93, 1.07)
Women							
Total cardiovascular disease							
Person–years	105,754	225,638	54,479	4363		172,652	217,581
Number of cases	198	431	156	24		286	523
Incident rate (per 1000 person–years)	1.87	1.91	2.86	5.50		1.66	2.40
Age-adjusted RR (95% CI)	1.0	1.09 (0.92, 1.29)	1.46 (1.19, 1.81)	1.63 (1.06, 2.49)	0.002	1.0	1.20 (1.04, 1.39)
Multivariate RR (95% CI)[a]	1.0	1.08 (0.92, 1.29)	1.38 (1.11, 1.70)	1.49 (0.97, 2.30)	0.02	1.0	1.18 (1.02, 1.37)
Multivariate RR (95% CI)[b]	1.0	1.08 (0.91, 1.28)	1.34 (1.08, 1.66)	1.43 (0.93, 2.21)	0.05	1.0	1.14 (0.98, 1.33)
Total cancer							
Person–years	89,850	190,889	46,545	3611		241,239	89,656
Number of cases	182	408	121	12		439	284
Incident rate (per 1000 person–years)	2.03	2.14	2.60	3.32		1.82	3.17
Age-adjusted RR (95% CI)	1.0	1.13 (0.95, 1.35)	1.33 (1.05, 1.67)	1.19 (0.66, 2.14)	0.32	1.0	1.29 (1.10, 1.50)
Multivariate RR (95% CI)[a]	1.0	1.14 (0.96, 1.36)	1.28 (1.02, 1.62)	1.07 (0.59, 1.93)	0.50	1.0	1.24 (1.06, 1.45)
Multivariate RR (95% CI)[b]	1.0	1.12 (0.94, 1.34)	1.22 (0.96, 1.55)	0.98 (0.54, 1.78)	0.63	1.0	1.22 (1.04, 1.43)
All causes							
Person–years	89,828	190,769	46,504	3611		258,315	72,397

Table 1 (*continued*)

	Degree of interest					Participation in screening	
	High Interest	Moderate +Interest	Low Interest	No Interest	*P* value for Trend	Yes	No
Women							
Number of cases	481	1053	369	57		1296	664
Incident rate (per 1000 person–years)	5.35	5.52	7.93	15.8		5.02	9.24
Age-adjusted RR (95% CI)	1.0	1.10 (0.99, 1.23)	1.44 (1.26, 1.65)	1.76 (1.33, 2.32)	<0.001	1.0	1.28 (1.16, 1.40)
Multivariate RR (95% CI)[a]	1.0	1.10 (0.99, 1.23)	1.36 (1.18, 1.56)	1.52 (1.15, 2.02)	<0.001	1.0	1.21 (1.09, 1.33)
Multivariate RR (95% CI)[b]	1.0	1.09 (0.98, 1.22)	1.31 (1.14, 1.51)	1.42 (1.07, 1.89)	0.004	1.0	1.15 (1.07, 1.28)

[a] Adjusted for age, body mass index, smoking status, alcohol intake, education, hours of walking, employment status, marital status, history of hypertension, history of diabetes family history of stroke, family history of coronary heart disease, and family history of cancer.
[b] Further adjustment for the degree of interest in screening and participation status.

and reduction of risk factor levels (Silagy et al., 1993). Other studies indicated that mortality rate was higher among non-participants in health screening compared to participants partly because non-participants were more likely to be smokers, heavy drinkers, or hypertensive (Puska et al., 1983; Hoffmeister et al., 1996). Furthermore, non-participants were less motivated to make lifestyle modification and showed lower compliance to medical treatment (Magnus et al., 1983; Thorogood et al., 1993). However, to our knowledge, there are no data on the effects of people's interest levels and participation in health screening activities in relation to risk of mortality. We therefore examined the relationship of interest levels and participation status with risks of mortality from CVD, cancer, and all causes in a large cohort study.

Methods

The JACC study enrolled 46,465 men and 64,327 women (aged 40 to 79) who attended to a screening program and responded to a questionnaire in 1988–1990, with considerably high response rate. Details of the study procedure was described elsewhere (Ohno et al., 2001; Tamakoshi et al., 2005). We used the participant's responses to two questions regarding screening: "What is your interest level in health screening?" and "Did you participate in past year in health screening program?" A total of 31,760 persons were excluded from analyses because the participation on screening and/or on interest level were not surveyed, and 3998 persons due to previous history of stroke, coronary heart disease, or cancer at baseline. Therefore, 28,530 men and 40,295 women were included in the present analysis. Follow-up was conducted until December 31, 1999, and the average follow-up period was 9.7 years. The Ethical Committees of Nagoya University and University of Tsukuba approved the present study.

The associations between interest level (high = 3, moderate = 2, low = 1, and no = 0), participation status (yes = 1 and no = 0), and a combination of these two variables and time to death from CVD (ICD-9 codes 390–459, ICD-10 codes I01–I99), cancer (140–208, C00–C97), and all causes were analyzed separately in the two sexes. Cox proportional hazards regression model was used to calculate the relative risks (RR) and 95% confidence intervals (95% CI) for the relation between interest level, participation status, and a combination of these two variables and risk of mortality from CVD, cancer, and all causes. The adjustment variables are listed in the footnotes of the tables. Furthermore, to reduce the potential effects of as-yet-undiagnosed diseases at baseline, we performed analyses after the exclusion of deaths during the first 2 years of follow-up.

Results

Women were 3 years older than those who reported no-interest or no-participation in screening, but such a trend was not observed for men. Men and women who reported low or no interest or no participation in screening were likely to be sedentary, current smokers, and unemployed, and to have higher ethanol intake. History of hypertension and family histories of stroke and cancer were less prevalent in categories of low- or no-interest level or no-participation in screening compared with high-interest levels or participation.

Table 1 shows the sex-specific, age- and multivariate-adjusted relative risks of mortality from CVD, cancer, and all causes according to interest level and participation status. Men with no interest had 1.5- to 2.0-fold higher mortality from CVD, cancer, and all causes compared to those with high interest. Similar associations for CVD and all-cause mortality were found in women. There was no difference in mortality risks between men who had not participated in screening and those who had participated. Women who had not participated had approximately 1.2-fold higher mortality from CVD, cancer, and all causes compared to those who had participated. Further adjustment for known risk factors did not substantially alter these associations.

Table 2 shows the sex-specific, multivariate-adjusted relative risks of cardiovascular disease, cancer, and all-cause mortality according to the combination of the interest level and participation status. Men who reported lower interest and participated had 1.2- to 1.4-fold higher mortality from CVD and all causes, and for women, 1.4-fold higher mortality from all causes compared to those who had higher interest and had participated. A similar excess risk of mortality was found among men with lower interest but participation in health screening, but such a trend was less evident among women.

We repeated the analyses after excluding deaths during the first 2 years of follow-up to eliminate the potential effects of as-yet-undiagnosed diseases on the associations, but found no substantial change in the associations. For example, the relative risks of mortality from CVD for persons with no interest vs. high interest were 1.88 (1.30–2.73) among men and 1.21 (0.74–2.00) among women. Relative risks of mortality from CVD for non-participation were 1.02 (0.88–1.18) among men and 1.15 (0.98–1.36) among women.

Discussion

In the present large prospective study, there was a significant association between lower interest in health screening and higher mortality from CVD and all causes for both sexes. Among women, but not men, non-participation in health screening was associated with 18–24% excess risk of mortality from CVD, cancer, and all causes. There was 23–47% excess risk of mortality from CVD and all causes among those with lower interest and non-participation in health screening in both sexes. A similar excess risk of mortality was found among men with lower interest but participation in health screening, but such a trend was less evident for women.

Table 2
Sex-specific multivariate relative risks and 95% confidence intervals of mortality from total cardiovascular disease, total cancer, and all causes according to the combination of interest and participation in screening

	Higher interest and participation	Lower interest and participation	Higher interest and no participation	Lower interest and no participation
Men				
Total cardiovascular disease				
Person–years	114,542	15,501	105,960	34,447
Number of cases	367	57	427	161
Incident rate (per 1000 person–years)	3.20	3.68	4.03	4.67
Multivariate RR (95% CI)	1.0	1.35 (1.02, 1.79)	1.02 (0.88, 1.17)	1.36 (1.10, 1.61)
Total cancer				
Person–years	131,008	20,813	89,575	29,194
Number of cases	676	114	527	167
Incident rate (per 1000 person–years)	5.16	5.48	5.88	5.72
Multivariate RR (95% CI)	1.0	1.17 (0.96, 1.43)	1.09 (0.98, 1.23)	1.13 (0.95, 1.34)
All causes				
Person–years	158,812	26,031	61,689	23,917
Number of cases	2,035	373	878	390
Incident rate (per 1000 person–years)	12.8	14.3	14.2	16.3
Multivariate RR (95% CI)	1.0	1.24 (1.10, 1.38)	1.01 (0.93, 1.09)	1.23 (1.10, 1.37)
Women				
Total cardiovascular disease	156,292	16,360	175,099	42,482
Person–years				
Number of cases	249	37	380	143
Incident rate (per 1000 person–years)	1.59	2.26	2.17	3.37
Multivariate RR (95% CI)	1.0	1.29 (0.91, 1.82)	1.15 (0.97, 1.35)	1.47 (1.19, 1.82)
Total cancer				
Person–years	214,990	26,249	65,749	23,907
Number of cases	383	56	207	77
Incident rate (per 1000 person–years)	1.78	2.13	3.15	3.22
Multivariate RR (95% CI)	1.0	1.14 (0.86, 1.52)	1.24 (1.04, 1.48)	1.33 (1.03, 1.71)
All causes				
Person–years	229,131	29,184	51,466	20,931
Number of cases	1093	203	441	223
Incident rate (per 1000 person–years)	4.77	6.96	8.57	10.7
Multivariate RR (95% CI)	1.0	1.27 (1.09, 1.48)	1.17 (1.05, 1.32)	1.43 (1.24, 1.66)

Categories for multivariate adjustment were as follows: age, body mass index, smoking status, alcohol intake, education, hours of walking, employment status, marital status, history of hypertension, history of diabetes, family history of stroke, family history of coronary heart disease, and family history of cancer.

Previous studies suggested that individual motivation to change unhealthy behaviors could enhance the modification of risk factors following health screening (Magnus et al., 1983; Thorogood et al., 1993). In other studies, persons who had a high value on their health were more likely to attend health screening (Norman, 1993, 1995). We found that persons with the lowest interest level in health screening were more likely to be sedentary and current smokers and have high ethanol intake compared with those with higher interest levels. Furthermore, persons who had not participated in health screening were more likely to have harmful lifestyles than those who had participated. Thus, we assume that persons with lower interest levels in health screening or no participation in screening have lower value on their health and lower motivation to modify their risk behaviors than those with higher interest level.

This is the first epidemiologic study to examine the relations of interest levels and participation in health screening with risks of cause-specific mortality. The present study suggests that both interest levels and participation in health screening have an effect on health for women. However, interest levels but not participation may influence men's health. This may be because men are less serious about their results of health screenings and less likely to modify their unhealthy behaviors even when they participate in health screenings.

The present study has several limitations. First, there would be residual confounding on the association of interest levels and participation status with risk of mortality, although we adjusted for selected risk factors. Second, individuals with illnesses that negatively influenced participation in screening may have increased the risk of mortality. This possibility, however, is unlikely because the participation–mortality association did not change after excluding early deaths.

In conclusion, men and women with lower interest and women with no participation in health screening were at high risk for CVD and all-cause mortality. Additionally, men who participated but had lower interest in health screening are also considered as high risk for CVD. To raise the interest in health screening may be important for individuals to modify their unhealthy behaviors in prevention of cardiovascular disease.

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(3) 両親の死亡年齢と本人の死亡リスクとの関連

目的：両親の死亡年齢が、本人の死亡リスクに及ぼす影響について、コホート研究により明らかにすることを目的とした。

方法：文部科学省大規模コホートでの対象者に対し、1989 年から 1990 年に質問紙により調査を行い、両親の生死の質問項目に回答した者（父親の死亡年齢に関する分析では 53,906 人、母親に関する分析では 55,988 人）、両親の死亡年齢と本人の死亡との関連を分析した。年齢、喫煙、飲酒、主観的ストレス等を調整した相対危険度を算出した。

結果：両親の死亡年齢が 60 歳未満に対して、死亡年齢が 80 歳以上での相対危険度（95%CI）は、男の循環器疾患では 0.7(0.6-0.8)、がんでは 0.9(0.8-1.0)、全死亡では 0.8(0.8-0.9)であった。女ではそれぞれ 0.8(0.7-1.0)、0.8(0.6-0.9)、0.8(0.7-0.9)であった。母親の死亡年齢が 65 歳未満に対して、死亡年齢が 85 歳以上での相対危険度は、男の循環器疾患では 0.7(0.6-0.9)、がんでは 1.0(0.9-1.2)、全死亡では 0.9(0.9-1.0)であった。女ではそれぞれ 0.8(0.6-0.9)、1.0(0.8-1.2)、0.8(0.7-0.9)であった。

考察：両親の死亡年齢、特に父親の死亡年齢が低い者については、特に循環器疾患・がん予防のための保健対策が必要であると推察された。

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Parental longevity and mortality amongst Japanese men and women: the JACC Study

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Abstract. Ikeda A, Iso H, Toyoshima H, Kondo T, Mizoue T, Koizumi A, Inaba Y, Tamakoshi A, JACC Study Group (University of Tsukuba, Ibaraki; Nagoya University Graduate School of Medicine, Nagoya; University of Occupational and Environmental Health, Fukuoka; Kyoto University, Kyoto; Juntendo University School of Medicine, Tokyo; and Nagoya University Graduate School of Medicine, Nagoya; Japan). Parental longevity and mortality amongst Japanese men and women: the JACC Study. *J Intern Med* 2006; **259**: 285–295.

Objectives. To examine whether the risk of mortality varies according to parents' age at death.

Design and subjects. A large prospective study in Japanese men and women from 45 communities across Japan. A total of 51 485 men and women aged 40–79 years completed self-administered questionnaires at baseline and followed up for 9.6 years.

Results. The risk of mortality from stroke, cardiovascular disease, and all causes was 20–30% lower in men and women with fathers who died at age ≥80 years, compared with those with fathers whose age at death was <60 years. A similar reduction was found when the age at death of mothers was ≥85 years compared with <65 years. Furthermore, the risk reduction was more evident amongst persons with both parents being long-lived parents compared with those with being short-lived parents, especially for death from cardiovascular disease.

Conclusions. Our findings indicate that parental longevity could be a predictor for reduced risk of mortality from stroke, cardiovascular disease, and all causes for both Japanese men and women.

Keywords: Asian, offspring mortality, parental longevity.

Introduction

Longevity in humans is determined by a combination of the individual's environment and its interaction with genes coding for resistance and long survival [1, 2]. The effect of parental longevity on the general and cause-specific mortality in sons and daughters has been examined in the US [3–5] and Europe [6–8]. These studies showed that individuals with short-lived parents had a higher risk of mortality than those with long-lived parents [3–8].

Japan is recognized as a country with the longest healthy life expectancy, for men and women, in the world [9]. However, no study has yet examined the association between parental longevity and mortality in Japan. It is of great importance to examine whether the parental longevity, which may be

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associated with offspring's socio-economic factors such as occupational class [7] and lifestyle factors such as smoking habit and alcohol consumption [5], leads to the reduced risk of mortality.

A study with a large cohort of subjects would permit clarification of the relative contributions of parental longevity on the specific causes of mortality amongst offspring. We hypothesized that the risk of mortality from cardiovascular disease, cancer, respiratory disease, infections, external causes (injuries, poisoning and other lesions), and all causes, is higher in individuals with short-lived parents compared with those with long-lived parents. Therefore, we examined the relationship between parental longevity and the risk of mortality in a large cohort study.

Methods

This study examined 110 792 subjects (46 465 men and 64 327 women, aged 40–79 years) who participated in the Japan Collaborative Cohort Study for Evaluation of Cancer Risk Sponsored by the Ministry of Education, Science, Sports and Culture (JACC Study). Between 1988 and 1990, individuals living in 45 communities across Japan were enrolled in this study and completed self-administered questionnaires including those on lifestyle and medical histories of cardiovascular disease and cancer at study baseline. Details of study procedure have been described elsewhere [10]. Informed consent was obtained from all subjects prior to questionnaire completion. We used participant's responses to questions: 'Is your father and/or mother still alive (no or yes)?', 'How old was your father and/or mother when he and/or she passed away?' and 'How old is he and/or she if he and/or she are alive?' A total of 5824 men and 7351 women were excluded from the analysis because the question on parental age of death was omitted in six communities (12%). A total of 36 449 men and 51 365 women provided valid responses to these questions; response rates of these questions were 90% for both men and women. Then, we excluded 12 868 men and 17 064 women who reported father as alive and aged <80 years for the analysis of paternal longevity, and 12 096 men and 15 754 women who reported mother as alive and aged <85 years for the analysis of maternal longevity as we were not able to group those into the categories of parental age of death. We also excluded 1753 men and 2223 women from the analysis due to previous history of stroke, coronary heart disease or cancer at study baseline. Therefore, a total of 21 828 men and 32 078 women were used for the analysis of paternal longevity and a total of 22 600 men and 33 388 women were used for the analysis of maternal longevity.

Mortality surveillance

The subjects were followed from the date of the acceptance of the baseline survey through 31 December 1999. As the information of the resident register is open to general public under the resident registration law, investigators confirmed yearly residence status and survival using residential registers, kept by a public health centre in each of the study areas. Residency and death registration is required by Family Registration Law in Japan, and was believed to be complete across Japan. Death certificate diagnoses were provided by the Ministry of Health and Labor under permission from Welfare after Ministry of Internal Affairs and Communications granted permission where the underlying causes of deaths were defined according to the *International Classification of Diseases*, 9th Revision from 1988 to 1994, and 10th Revision from 1995 to 1999 for the National Vital Statistics. Therefore, all deaths that occurred in the cohort were confirmed by death certificates from a public health centre, except for subjects who died after they moved from their original community, in which case the subject was treated as a censored case. The average follow-up period for the participants was 9.6 years. The Ethical Committees of the Nagoya University School of Medicine and the University of Tsukuba approved the present study.

Statistical analysis

Age-adjusted mean values and proportions of selected mortality risk factors were presented according to the categories of age at death of fathers: <60, 60–69, 70–79 and ≥80 years, and of mothers: <65, 65–70, 70–75 and ≥85 years. Alive fathers aged ≥80 and mothers aged ≥85 were categorized as the highest age groups. Statistical testing for differences of selected mortality risk factors amongst the categories of age at death of parents was conducted using analysis of covariance.

The person-time for each participant were calculated from the date of the completed baseline questionnaire on 1989 until the time of death or withdrawal from study, or 31 December 1999. Cox proportional hazards modelling was used to determine whether age of parents was significantly associated with stroke (ICD-9 codes 430–438, ICD-10 codes I60–I69), coronary heart disease (410–414, I20–I25), cardiovascular disease (390–459, I01–I99), cancer (140–208, C00–C97), respiratory disease (460–519, J00–J99), infections (001–139, A00–B99), external causes (800–999, S00–T98), and all causes. We compared the sex-specific mortality rates for persons whose fathers' age of death were 60–69, 70–79, and ≥80 to those whose fathers' age of death was <60. For maternal age of death, categories 5 years higher than those for fathers' age of death were used because the average life expectancy was approximately 5–7 year higher for women than for men [9]. Relative risks with 95% confidence intervals were calculated after adjustment for age and potential confounders. The confounding variables, that were associated with both mortality and the categories of parental age, were included in the multivariate analysis. These variables were current age as time-dependent variable, smoking status (never, ex-smoker, and current smokers of 1–19 and >20 cigarettes per day), alcohol intake (never, ex-drinker, and current drinker of ethanol at 1–22, 23–45, 46–68 and >69 g day^{-1}), marital status (married, widowed, divorced, or single), education (<13, 13–15, 16–18 and >19 years), employment status (employed vs. unemployed), level of perceived stress (low, medium and high), history of hypertension (no or yes), and history of diabetes (no or yes). For further analysis, we examined the mortality rates for persons who had long-lived parents (fathers' age ≥80 and mothers' age ≥85), those who had a long-lived father and short-lived mother, those who had a long-lived mother and short-lived father, compared with those having short-lived parents (fathers' age <80 and mothers' age <85). We tested the assumption of proportional hazards according to the age of parental death which was tested by using both time-dependent covariate method and linear correlation test, and found no violation for proportionality. All analyses were conducted using the SAS statistical package (Version 8.2; SAS Institute Inc., Cary, NC, USA).

Results

Separately, we examined the four categories of parental age in relation to selected mortality risk factors for men and women (Table 1). Men with fathers who survived for ≥80 years were approximately 1 year younger and those with mothers who survived for ≥85 years were approximately 2 years older, and were more likely to be educated, employed and less hypertensive than those whose fathers survived for <60 years or mothers survived for <65 years. Men whose fathers survived for ≥80 years had lower ethanol intake and were less likely to be current smokers, compared with those whose fathers survived for <60 years. In contrast, this difference was not found amongst men whose mothers survived for ≥85 years compared with those whose mothers survived for <65 years.

Women with fathers who survived for ≥80 years were approximately 1 year younger and those with mothers who survived for ≥85 were approximately 2 years older, and were more likely to be educated and were less likely to be hypertensive and current smokers, compared with those whose fathers survived for <60 years or mothers survived for <65 years. Women with fathers who survived for ≥80 years were more likely to be employed compared with those whose fathers survived for <60 years; however, this difference was not observed amongst women whose mothers survived for ≥85 years compared with those whose mothers survived for <65 years. Women with mothers who survived for ≥85 years, compared with those whose mothers survived for <65 years were less likely to be diabetic patients, had lower ethanol intake and stress, and were more likely to be married. However, no such differences were found amongst women whose fathers survived for ≥80 years compared with those whose fathers survived for <60 years.

During 520 202 person-years of follow-up for the analysis of paternal longevity, the identified number of deaths from stroke was 992 (537 men, 455 women), coronary heart disease 403 (247 men, 156 women), cardiovascular disease 2060 (1149 men, 911 women), cancer 2586 (1619 men, 967 women), respiratory disease 732 (518 men, 214 women), infections 104 (59 men, 45 women), external causes 465 (264 men and 201 women) and all causes 6742 (4035 men, 2707 women). For the maternal longevity analysis of 540 409

Table 1 Sex-specific age-adjusted mean values or prevalence of mortality risk factors at baseline according to the parents' age of death

	Father's age of death					Mother's age of death				
	Age < 60	60 ≤ age < 70	70 ≤ age < 80	Age ≥ 80	P-value	Age < 65	65 ≤ age < 75	75 ≤ age < 85	Age ≥ 85	P-value
Men										
No. at risk	4943	4751	6110	6024		6623	4551	6339	5087	
Age (year)	62.0	62.3	61.9	61.3	<0.001	61.4	61.3	62.3	63.1	<0.001
History of hypertension (%)	27.3	28.3	26.2	21.5	<0.001	27.9	27.5	24.9	22.5	<0.001
History of diabetes (%)	8.1	7.5	7.8	7.8	0.83	7.9	7.6	8.2	7.6	0.70
Ethanol intake (g day^{-1})	34.4	34.2	34.2	32.4	<0.001	34.2	33.2	33.9	33.4	0.19
College or higher education (%)	13.2	12.5	12.5	14.0	0.06	12.8	12.3	13.0	14.6	0.006
Employed (%)	71.1	73.5	75.4	75.7	<0.001	72.3	73.3	74.5	75.8	<0.001
Married (%)	93.1	93.5	94.2	93.9	0.17	93.3	94.0	93.7	94.0	0.40
High stress (%)	19.1	17.8	18.6	17.8	0.35	18.4	18.6	17.5	17.6	0.48
Current smoker (%)	51.0	52.7	52.2	50.0	0.03	50.8	52.1	52.1	52.3	0.32
Women										
No. at risk	7525	7036	8782	8735		10 011	6751	8975	7651	
Age (year)	61.6	61.9	61.6	61.0	<0.001	60.9	60.9	61.9	62.5	<0.001
History of hypertension (%)	30.3	30.0	28.1	26.3	<0.001	30.5	30.2	27.7	22.8	<0.001
History of diabetes (%)	5.5	5.1	4.9	4.6	0.09	5.2	5.7	4.7	4.6	0.02
Ethanol intake (g day^{-1})	10.9	9.9	9.7	9.6	0.11	10.3	10.9	9.6	8.9	0.01
College or higher education (%)	6.1	5.8	7.1	7.5	<0.001	6.2	6.4	6.6	8.0	<0.001
Employed (%)	30.8	31.5	32.9	33.2	0.007	31.7	31.6	32.6	32.7	0.29
Married (%)	79.5	79.4	80.1	80.1	0.56	78.3	79.3	81.1	80.5	<0.001
High stress (%)	17.8	16.8	17.0	17.2	0.52	18.0	16.6	16.8	16.5	0.04
Current smoker (%)	5.2	4.8	4.4	4.3	0.04	5.1	4.8	4.3	4.1	0.01

person-years of follow-up, the respective number of deaths were 1009 (545 men, 464 women), 410 (252 men, 158 women), 2107 (1167 men, 935 women), 2709 (1699 men, 1010 women), 751 (532 men, 219 women), 105 (59 men, 46 women), 475 (274 men, 201 women) and 6964 (4180 men, 2784 women).

Table 2 shows sex-specific relative risks of mortality from stroke, coronary heart disease, cardiovascular disease, cancer, respiratory disease, infectious disease, external causes, and all causes according to age at death of fathers. In model with age adjusted only, men with fathers who survived for ≥80 years had a 15–38% reduction in the risk of mortality from stroke, coronary heart diseases, cardiovascular disease, cancer, and all causes compared with those whose fathers survived for <60 years. Women whose fathers survived for ≥80 years had a 20–38% reduction in the risk of mortality from stroke, cardiovascular disease, cancer, respiratory disease, and all causes compared with those whose fathers survived for <60 years. These associations did not alter materially even after adjustment for potential confounding variables.

Table 3 shows the data according to age at death of mothers. Similar to the results from the analysis of paternal age, we found reductions in the risk of mortality from stroke, cardiovascular disease, and all causes for both men and women whose mothers survived for ≥85 years compared with those whose mothers survived for <65 years.

In order to determine whether the importance of parental survival decreased with age, we conducted a stratified analysis by age subgroups. However, the associations between parental survival and mortality did not vary between age subgroups (data not shown). For example, multivariable relative risks (95% CI) of mortality from cardiovascular disease for persons whose fathers survived for <60 years vs. ≥80 years were 0.75 (0.55–1.04) amongst men aged 40–64 years and 0.67 (0.55–0.82) amongst men aged >65 years (*P*-value for interaction = 0.66); 0.72 (0.46–1.12) amongst women aged 40–64 years and 0.85 (0.69–1.06) amongst women aged >65 years (*P*-value for interaction = 0.49). The multivariable risks for the age at death of mother was 0.61 (0.44–0.86) amongst men aged 40–64 years and 0.76 (0.62–0.92) amongst men aged >65 years (*P*-value for interaction = 0.87); 0.87 (0.56–1.34) amongst women aged 40–64 years and 0.76 (0.62–0.94) amongst women aged >65 years (*P*-value for interaction = 0.40).

Table 4 shows sex-specific multivariable-adjusted relative risks of stroke, coronary heart disease, cardiovascular disease, cancer, respiratory disease, infectious disease, external causes, and all-cause mortality according to the combination of the age at death of father and of mother. We found a 17–47% reduction in the risk of mortality from stroke, cardiovascular disease, and all causes amongst both men and women who had long-lived parents compared with those with short-lived parents. There was a 15–30% reduction in the risk of mortality from stroke, coronary heart disease, cardiovascular disease, and all causes for both men and women with long-lived fathers and short-lived mothers. Furthermore, there was a 8–40% reduction in the risk of mortality from stroke, cardiovascular disease, and all causes for both men and women with long-lived mothers and short-lived fathers.

Discussion

We found that individuals with a father or mother surviving into old age had a lower risk of mortality from stroke, cardiovascular disease, and all causes. The association, mainly for cardiovascular disease, was more evident for individuals with both a long-lived father and mother. The association appeared to be statistically independent of various mortality risk factors.

Japan is recognized as a country with the longest life expectancy for both men (78 years) and women (85 years), and the biggest gap in life expectancy between men and women in the world [9]. In the present study, 33.5% of mothers were still alive at the time of the baseline investigation, as opposed to only 16.4% of the fathers. According to a previous study, the age of 85 years could be considered as a threshold age for female longevity, but the demarcation point could be much lower for male longevity [11]. Therefore, we used different cut-off points for the age at death of fathers and mothers.

To our knowledge, there are no studies that examined the association between parental longevity and cause-specific mortality in offspring with different cut-points for the age at death of fathers and mothers. In the present study, we found consistent associations between paternal and maternal longevity and offspring's risk of mortality from

Table 2 Sex-specific relative risks (RR) and 95% confidence intervals (95% CI) of mortality from stroke, coronary heart disease, cardiovascular disease, cancer, respiratory disease, infections, external causes and all causes according to father's age at death

Father's age of death	Men				*P*-value for trend	Women				*P*-value for trend
	Age < 60	60 ≤ age < 70	70 ≤ age < 80	Age ≥ 80		Age < 60	60 ≤ age < 70	70 ≤ age < 80	Age ≥ 80	
Person-years	46 103	44 488	57 499	57 774		72 910	68 534	86 440	86 455	
Stroke	140	128	163	106		117	116	129	93	
RR (95% CI)[a]	1.0	0.91 (0.72–1.16)	0.94 (0.75–1.18)	0.64 (0.50–0.82)	0.005	1.0	0.99 (0.77–1.28)	0.92 (0.72–1.18)	0.72 (0.55–0.95)	0.06
RR (95% CI)[b]	1.0	0.90 (0.70–1.14)	0.95 (0.76–1.19)	0.68 (0.52–0.87)	0.02	1.0	1.01 (0.78–1.30)	0.93 (0.72–1.19)	0.75 (0.57–0.98)	0.09
Coronary heart disease	61	67	74	45		38	44	47	27	
RR (95% CI)[a]	1.0	1.10 (0.78–1.56)	0.98 (0.70–1.37)	0.62 (0.42–0.91)	0.009	1.0	1.15 (0.74–1.77)	1.03 (0.67–1.58)	0.65 (0.40–1.07)	0.06
RR (95% CI)[b]	1.0	1.10 (0.78–1.56)	1.00 (0.71–1.41)	0.66 (0.45–0.98)	0.03	1.0	1.18 (0.76–1.82)	1.05 (0.68–1.61)	0.68 (0.41–1.12)	0.07
Cardiovascular disease	299	279	341	230		222	243	253	193	
RR (95% CI)[a]	1.0	0.93 (0.79–1.10)	0.92 (0.79–1.07)	0.65 (0.55–0.77)	<0.001	1.0	1.09 (0.91–1.31)	0.95 (0.80–1.14)	0.80 (0.66–0.97)	0.005
RR (95% CI)[b]	1.0	0.92 (0.78–1.08)	0.93 (0.80–1.09)	0.69 (0.58–0.82)	<0.001	1.0	1.11 (0.92–1.33)	0.96 (0.80–1.15)	0.83 (0.68–1.00)	0.009
Cancer	398	370	443	408		255	243	250	219	
RR (95% CI)[a]	1.0	0.94 (0.82–1.08)	0.89 (0.78–1.02)	0.85 (0.74–0.98)	0.38	1.0	0.98 (0.82–1.17)	0.82 (0.69–0.98)	0.76 (0.63–0.91)	0.02
RR (95% CI)[b]	1.0	0.94 (0.81–1.08)	0.90 (0.79–1.03)	0.87 (0.76–1.00)	0.61	1.0	0.98 (0.82–1.16)	0.82 (0.69–0.97)	0.76 (0.63–0.91)	0.02
Respiratory disease	129	122	147	120		62	51	59	42	
RR (95% CI)[a]	1.0	0.93 (0.73–1.19)	0.92 (0.73–1.17)	0.80 (0.62–1.02)	0.40	1.0	0.81 (0.56–1.18)	0.79 (0.55–1.13)	0.62 (0.42–0.92)	0.36
RR (95% CI)[b]	1.0	0.93 (0.72–1.19)	0.92 (0.73–1.17)	0.82 (0.64–1.05)	0.55	1.0	0.81 (0.56–1.17)	0.78 (0.55–1.12)	0.62 (0.42–0. 6.92)	0.39
Infections	11	11	15	22		14	11	14	6	
RR (95% CI)[a]	1.0	1.01 (0.44–2.32)	1.10 (0.50–2.39)	1.67 (0.81–3.45)	0.28	1.0	0.79 (0.36–1.74)	0.83 (0.39–1.73)	0.38 (0.15–0.98)	0.24
RR (95% CI)[b]	1.0	1.03 (0.45–2.38)	1.09 (0.50–2.37)	1.66 (0.80–3.43)	0.30	1.0	0.79 (0.36–1.74)	0.85 (0.40–1.79)	0.38 (0.15–1.00)	0.24
External causes	55	80	67	62		45	47	58	51	
RR (95% CI)[a]	1.0	1.48 (1.05–2.09)	0.98 (0.68–1.39)	0.92 (0.64–1.32)	0.007	1.0	1.08 (0.72–1.62)	1.08 (0.73–1.59)	0.99 (0.66–1.48)	0.89
RR (95% CI)[b]	1.0	1.49 (1.05–2.10)	0.99 (0.69–1.41)	0.96 (0.67–1.39)	0.01	1.0	1.07 (0.71–1.61)	1.07 (0.73–1.59)	0.99 (0.66–1.47)	0.89
All causes	989	965	1141	940		702	678	731	596	
RR (95% CI)[a]	1.0	0.98 (0.90–1.07)	0.93 (0.85–1.01)	0.80 (0.73–0.87)	<0.001	1.0	0.98 (0.88–1.08)	0.87 (0.78–0.96)	0.76 (0.68–0.85)	<0.001
RR (95% CI)[b]	1.0	0.98 (0.89–1.07)	0.94 (0.86–1.02)	0.83 (0.76–0.90)	<0.001	1.0	0.98 (0.88–1.09)	0.87 (0.79–0.97)	0.78 (0.70–0.87)	0.007

[a]Adjusted for age (time-dependent covariate). [b]Adjusted for age (time-dependent covariate), smoking status, alcohol intake, perceived mental stress, history of hypertension, history of diabetes, educational status, employment status and marital status.

Table 3 Sex-specific relative risks (RR) and 95% confidence intervals (95% CI) of mortality from stroke, coronary heart disease, cardiovascular disease, cancer, respiratory disease, infections, external causes and all causes according to mother's age at death

Mother's age of death	Men				*P*-value for trend	Women				*P*-value for trend
	Age < 65	65 ≤ age < 75	75 ≤ age < 85	Age ≥ 85		Age < 65	65 ≤ age < 75	75 ≤ age < 85	Age ≥ 85	
Person-years	62 333	42 858	59 750	48 239		97 749	66 128	88 171	75 181	
Stroke	185	119	158	83		136	100	149	79	
RR (95% CI)[a]	1.0	0.96 (0.76–1.20)	0.87 (0.70–1.07)	0.54 (0.41–0.69)	<0.001	1.0	1.06 (0.82–1.37)	1.14 (0.90–1.44)	0.70 (0.53–0.92)	0.001
RR (95% CI)[b]	1.0	0.92 (0.73–1.16)	0.86 (0.70–1.07)	0.58 (0.44–0.76)	0.005	1.0	1.05 (0.81–1.36)	1.19 (0.94–1.50)	0.75 (0.56–1.01)	0.007
Coronary heart disease	80	53	73	46		42	39	47	30	
RR (95% CI)[a]	1.0	0.98 (0.69–1.39)	0.92 (0.67–1.27)	0.68 (0.48–0.98)	0.16	1.0	1.32 (0.86–2.05)	1.16 (0.77–1.76)	0.86 (0.54–1.37)	0.19
RR (95% CI)[b]	1.0	0.96 (0.68–1.35)	0.94 (0.69–1.29)	0.78 (0.53–1.15)	0.57	1.0	1.31 (0.85–2.03)	1.20 (0.80–1.82)	0.93 (0.57–1.52)	0.39
Cardiovascular disease	371	247	340	209		282	214	267	172	
RR (95% CI)[a]	1.0	0.99 (0.84–1.16)	0.93 (0.80–1.08)	0.67 (0.57–0.80)	<0.001	1.0	1.09 (0.91–1.30)	0.99 (0.83–1.17)	0.73 (0.61–0.89)	<0.001
RR (95% CI)[b]	1.0	0.97 (0.83–1.14)	0.94 (0.81–1.08)	0.74 (0.62–0.89)	0.02	1.0	1.09 (0.91–1.30)	1.01 (0.86–1.20)	0.75 (0.62–0.92)	0.002
Cancer	495	298	503	403		294	223	257	236	
RR (95% CI)[a]	1.0	0.89 (0.77–1.02)	1.03 (0.91–1.16)	0.97 (0.85–1.11)	0.13	1.0	1.11 (0.93–1.32)	0.92 (0.78–1.09)	0.97 (0.82–1.15)	0.11
RR (95% CI)[b]	1.0	0.88 (0.77–1.02)	1.03 (0.91–1.16)	0.99 (0.86–1.15)	0.12	1.0	1.11 (0.94–1.32)	0.92 (0.78–1.09)	0.95 (0.79–1.15)	0.09
Respiratory disease	147	112	148	125		84	43	49	43	
RR (95% CI)[a]	1.0	1.15 (0.90–1.46)	1.04 (0.83–1.31)	1.04 (0.82–1.31)	0.68	1.0	0.73 (0.50–1.05)	0.61 (0.43–0.86)	0.62 (0.43–0.89)	0.63
RR (95% CI)[b]	1.0	1.18 (0.92–1.50)	1.07 (0.85–1.35)	1.10 (0.86–1.42)	0.75	1.0	0.74 (0.51–1.06)	0.59 (0.41–0.84)	0.62 (0.42–0.91)	0.54
Infections	14	9	22	14		10	9	18	9	
RR (95% CI)[a]	1.0	0.95 (0.41–2.19)	1.59 (0.81–3.10)	1.19 (0.57–2.50)	0.39	1.0	1.30 (0.53–3.20)	1.87 (0.86–4.05)	1.07 (0.44–2.64)	0.36
RR (95% CI)[b]	1.0	0.87 (0.38–2.00)	1.49 (0.77–2.89)	1.38 (0.65–2.91)	0.39	1.0	1.33 (0.54–3.27)	1.92 (0.89–4.18)	1.31 (0.51–3.33)	0.54
External causes	92	50	72	60		58	44	58	41	
RR (95% CI)[a]	1.0	0.79 (0.56–1.12)	0.79 (0.58–1.08)	0.79 (0.57–1.09)	1.00	1.0	1.11 (0.75–1.64)	1.06 (0.73–1.52)	0.85 (0.57–1.27)	0.44
RR (95% CI)[b]	1.0	0.79 (0.56–1.10)	0.80 (0.59–1.08)	0.82 (0.57–1.18)	0.98	1.0	1.11 (0.76–1.63)	1.03 (0.72–1.47)	0.89 (0.58–1.37)	0.63
All causes	1232	805	1226	917		836	618	760	570	
RR (95% CI)[a]	1.0	0.97 (0.88–1.06)	1.01 (0.93–1.09)	0.89 (0.81–0.97)	0.01	1.0	1.07 (0.96–1.19)	0.95 (0.86–1.05)	0.82 (0.73–0.91)	<0.001
RR (95% CI)[b]	1.0	0.96 (0.88–1.05)	1.02 (0.94–1.10)	0.93 (0.85–1.02)	0.15	1.0	1.08 (0.97–1.19)	0.96 (0.87–1.06)	0.83 (0.74–0.93)	<0.001

[a]Adjusted for age (time-dependent covariate). [b]Adjusted for age (time-dependent covariate), smoking status, alcohol intake, perceived mental stress, history of hypertension, history of diabetes, educational status, employment status and marital status.

Table 4 Sex-specific relative risks (RR) and 95% confidence intervals (95% CI) of mortality from stroke, coronary heart disease, cardiovascular disease, cancer, respiratory disease, infections, external causes and all causes according to combination of father's and mother's age at death

	Men				Women			
	Father's age < 80 and mother's age < 85	Father's age ≥ 80 and mother's age < 85	Father's age < 80 and mother's age ≥ 85	Father's age ≥ 80 and mother's age ≥ 85	Father's age < 80 and mother's age < 85	Father's age ≥ 80 and mother's age < 85	Father's age < 80 and mother's age ≥ 85	Father's age ≥ 80 and mother's age ≥ 85
Person-years	126 832	38 109	21 257	16 121	193 346	58 702	34 537	22 997
Stroke	381	81	50	25	312	73	50	19
RR (95% CI)	1.0	0.70 (0.55–0.89)	0.60 (0.44–0.80)	0.53 (0.36–0.80)	1.0	0.77 (0.59–0.99)	0.68 (0.51–0.92)	0.56 (0.35–0.88)
Coronary heart disease	172	34	30	11	109	19	20	8
RR (95% CI)	1.0	0.65 (0.45–0.94)	0.79 (0.54–1.17)	0.53 (0.29–0.97)	1.0	0.58 (0.35–0.94)	0.78 (0.48–1.25)	0.68 (0.33–1.39)
Cardiovascular disease	787	171	132	56	612	151	106	45
RR (95% CI)	1.0	0.72 (0.61–0.85)	0.76 (0.63–0.91)	0.58 (0.44–0.76)	1.0	0.81 (0.68–0.97)	0.72 (0.59–0.89)	0.68 (0.50–0.92)
Cancer	1004	292	207	120	617	157	131	66
RR (95% CI)	1.0	0.94 (0.82–1.07)	0.99 (0.85–1.15)	0.93 (0.77–1.12)	1.0	0.81 (0.68–0.97)	0.95 (0.79–1.15)	0.90 (0.70–1.16)
Respiratory disease	322	85	76	36	142	34	30	8
RR (95% CI)	1.0	0.84 (0.66–1.07)	1.02 (0.79–1.31)	0.91 (0.64–1.28)	1.0	0.76 (0.52–1.10)	0.82 (0.55–1.22)	0.50 (0.25–1.03)
Infections	31	14	6	8	33	4	6	3
RR (95% CI)	1.0	1.44 (0.76–2.70)	0.90 (0.38–2.17)	1.87 (0.86–4.08)	1.0	0.38 (0.13–1.07)	0.79 (0.33–1.90)	0.82 (0.25–2.68)
External causes	169	45	33	18	129	31	21	12
RR (95% CI)	1.0	0.88 (0.63–1.22)	1.00 (0.69–1.46)	0.87 (0.53–1.41)	1.0	0.77 (0.52–1.13)	0.76 (0.48–1.20)	0.78 (0.43–1.42)
All causes	2585	678	510	270	1769	445	342	149
RR (95% CI)	1.0	0.85 (0.78–0.93)	0.92 (0.83–1.01)	0.83 (0.73–0.94)	1.0	0.81 (0.73–0.90)	0.83 (0.74–0.93)	0.74 (0.62–0.87)

Adjusted for age (time dependent covariate), smoking status, alcohol intake, perceived mental stress, history of hypertension, history of diabetes, educational status, employment status and marital status.

stroke, cardiovascular disease, and all causes. However, findings from previous prospective studies have been inconsistent. Several prospective studies reported that the maternal effect on offspring lifespan was stronger than the paternal effect [1–3, 12, 13]. In contrast, another study showed the paternal effect on offspring lifespan to be stronger than the maternal effect [5]. However, these studies used the same cut-off points for the age at death of fathers and mothers. Our results indicate that paternal and maternal longevity contributes equally to reduced mortality from stroke, cardiovascular disease and all causes for both sexes. The weak and inconsistent association between paternal and maternal longevity with offspring's mortality from cancer was consistent with the results of previous study [5].

In the present study, a potential protective effect of having parents surviving into old age could, in part, be attributed to economic and social advantages including education level and employment status between those with and without long-lived parents. Previous studies reported that both early and later life socio-economic disadvantages could contribute to increased risk of cardiovascular disease mortality [14–20]. We postulate that individuals with short-lived parents are more likely to become psychologically and economically unstable in their early and later life, which may influence their health behaviour, such as smoking and heavy drinking, thus raising the risk of mortality, especially from cardiovascular disease.

In the present study, unknown genetic factors could contribute to the reduced mortality associated with parental longevity. Candidate genes that have been implicated in longevity include apoE [21–23], angiotensin-converting enzyme (ACE) [22–24], histocompatibility locus antigen (HLA-DR) [23, 25], and plasminogen activator inhibitor 1 (PAI-1) [23, 26]. A certain mitochondrial DNA has been found more frequently in centenarians [23, 27]. These genetic influences could be modified by environmental factors, such as social, economical and lifestyle factors [1, 2, 28]. In addition to genetic factors, early family environment can have persistent effects on cardiovascular risk factors such as hypertension, smoking, alcohol consumption, low education and unemployment in adult life [29]. Hence, the early death of parents can be an indicator for their early environment that affects cardiovascular factors in adult life as well.

Some limitations of the present study warrant discussion. First, there would be residual confounding factors on the association between parental longevity and risk of mortality. Although we adjusted for various risk factors for mortality, we cannot exclude a possible influence from other risk factors and lifestyles. Secondly, there was no information on the age of the parents when they gave birth to the study subjects. A previous study reported that older parental age at reproduction was associated with higher mortality amongst offspring [11], in part due to higher risk of birth defects [30]. However, the number of deaths due to birth defects in our study population was small ($n = 16$) and our findings did not change after exclusion of these deaths. Thirdly, there might be a concern about selection bias as we excluded persons with alive fathers aged <80 and mothers aged <85 years from the analysis. When we analysed with data including these persons with alive fathers and mothers, the association did not change substantially. For example, multivariable relative risks (95% CI) of mortality from cardiovascular disease for persons whose fathers survived for <60 years vs. ≥80 years were 0.71 (0.60–0.83) amongst men and 0.85 (0.71–1.02) amongst women. The multivariable risks for maternal age were 0.75 (0.55–1.04) amongst men and 0.78 (0.64–0.94) amongst women.

The strength of our study is the prospective design and large sample size, leading to high statistical power for the detection of the effect of sex- and age-specific parental longevity on offspring mortality. We were also able to clarify the association with cause-specific mortality from cardiovascular disease, cancer, infections, external causes, as well as all-cause mortality.

In conclusion, our findings indicate that the longevity of parents, either fathers or mothers, could be a predictor for reduced risk of mortality from stroke, cardiovascular disease, and all causes for both Japanese men and women.

Conflict of interest statement

No conflict of interest was declared.

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