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Purpose in life (*Ikigai*) and employment status in relation to cardiovascular mortality: the Japan Collaborative Cohort Study

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ABSTRACT

Objectives To investigate whether having a purpose in life (*Ikigai*) is associated with risk of cardiovascular disease (CVD) mortality and whether the association varies by employment status.

Design Prospective cohort study.

Setting Residents in 45 municipalities, Japan.

Participants 29 517 men and 41 984 women aged 40–79 years, free of CVD and cancer at baseline from 1988 to 1990.

Primary outcome measures CVD mortality.

Results During the median follow-up of 19.1 years, 4680 deaths (2393 men and 2287 women) from total CVD were observed. Greater *Ikigai* was associated with a lower risk of CVD mortality, and the result was stronger for men than for women. Stratified by employment status, the inverse association was confined to unemployed persons. Among unemployed persons, the multivariable HRs of total CVD were higher for moderate and high versus low levels of *Ikigai*. Multivariable HRs (95% CIs) were 0.74 (0.57 to 0.97) and 0.69 (0.52 to 0.93), P for trend <0.044, respectively in men, and 0.78 (0.64 to 0.95) and 0.77 (0.61 to 0.97), P for trend=0.039 in women. No association was observed among the employed, including part-time workers, self-employed and homemakers for both men and women. Such an inverse association remained even after excluding early deaths within 5 years from the baseline survey.

Conclusion Higher levels of *Ikigai* were associated with a lower risk of CVD mortality, especially for unemployed men and women.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Strengths included a population-based cohort study, a large sample size and a long follow-up period.
⇒ Another strength was the adjustment for many confounding factors including lifestyle habits, social and psychological factors and medical histories such as hypertension and diabetes mellitus.
⇒ Limitation was a self-administered single-item questionnaire on the purpose in life (*Ikigai*) to assess exposure at the baseline survey.

INTRODUCTION

Recently, there has been growing evidence that positive psychological factors, such as life satisfaction, happiness, life enjoyment, optimism and purpose in life, have been associated with favourable health outcomes, including reduced risk of cardiovascular disease (CVD), in activities of daily living, cognitive impairment and all-cause mortality.[1–6] A meta-analysis of 17 studies (mainly from the USA, Canada and Europe) reported that psychological factors, such as meaning in life, purpose of life, life satisfaction, positive effect and self-esteem, were considered essential components of well-being.[7] In another meta-analysis, high life purpose was associated with a 17% lower risk of all-cause mortality and cardiovascular events such as myocardial infarction, cardiac death and stroke.[8]

'*Ikigai*' is a Japanese concept similar to 'purpose in life', 'meaning of life', 'life worth living' and 'reason to live', which can be translated as 'that which most makes one's life seem worth living'.[9] In Japanese, *Ikigai* is defined as a comprehensive concept related to life satisfaction, self-esteem, self-efficacy, morale and cognitive evaluation of the meaning of one's life.[10] *Ikigai* involves more than enjoyment, pleasure or happiness and provides significance for one's value in life, including subjective motivation for a living.[11] In a previous prospective cohort study of 43 391 Japanese adults over 7 years' follow-up, the presence of a sense of *Ikigai* was associated with decreased risk of all-cause and cardiovascular mortality among middle-aged and elderly Japanese men and women.[12] A panel study of 6739 US adults aged 53–105 years over a 4-year follow-up showed that a higher level of purpose in life was associated with a 22% reduced incidence of stroke after adjustment for age, gender, race/ethnicity and socioeconomic status.[13]

A meta-analysis of 42 cross-sectional and prospective cohort studies providing data on more than 20 million people showed that unemployment was associated with an increased risk of all-cause mortality, with a 63% higher risk for those who experienced unemployment than those who did not.[14] Unemployment status was associated with an increased incidence of cardiovascular events such as coronary heart disease and stroke associated with.[15–17] A study based on a population-wide dataset of 3 084 137 Belgian individuals aged 25–59 at the 2001 census showed that unemployment status was associated with health problems such as cardiovascular, endocrine and psychiatric disorders.[18] According to a study of 297 construction workers followed for 2 years, the longer the unemployment, the greater rise in blood pressure levels.[19] Poor health is a direct or indirect consequence of unemployment, and this causal relationship was mediated by health behaviours such as tobacco or alcohol consumption.[20–23]

No study, however, has focused on the impact of *Ikigai* on mortality risk by employment status. We hypothesise that *Ikigai* positively impacts cardiovascular health even in an unemployed situation. We aimed to test this hypothesis using a long-term follow-up of a large-scale prospective cohort study of Japanese adults.

METHODS

Study population

The Japan Collaborative Cohort Study for the Evaluation of Cancer Risks (JACC study) enrolled residents in 45 area around Japan between 1988 and 1990. Participants were required to conduct self-administered questionnaires about their lifestyle and medical history concerning CVD and cancer at baseline. The details of the study procedure are described elsewhere.[24] Briefly, a total of 110 585 subjects (46 395 men and 64 190 women) aged 40–79 years old participated in the JACC study at the baseline survey. Among the participants, 7692 were excluded due to a history of CVD or cancer at baseline. Additionally, 31 392 (25 730 participants in areas with no questions about *Ikigai* and 5662 participants who lacked information about *Ikigai*) were excluded. Finally, 71 501 participants (29 517 men and 41 984 women) were eligible for inclusion in the analyses (figure 1). Prior to the completion of the questionnaire, the participants were provided informed consent to be involved in this epidemiological study. Individual informed consent was obtained from each participant in 36 out of the 45 study areas (written consent in 35 areas and oral consent in 1 area). In the remaining 9 areas, group consent was obtained from each community representative.

Mortality surveillance

The date and cause of death for participants were determined by reviewing all death certificates from each area. According to the International Classification of Diseases, 10th revision, cause-specific mortality was defined within total CVD mortality (I01–I99). Type-specific CVD mortality was defined as I60.0–I69.8 for total stroke, I20.0–I25.5 for coronary heart disease, I50.0–I50.9 for heart failure and other CVDs. Total stroke was divided into three subtypes: cerebral infarction (I63.0–I63.9), haemorrhagic stroke (I60.0–I61.9) and stroke of undetermined type (I62.0–I62.9 and I64–I69.8). From baseline until 31 December 2009, a total of 15 801 participants were censored because of death, and 3986 were censored because they moved out of their original residential area; follow-up was terminated at the end of 1999 (four areas), 2003 (four areas) and 2008 (two areas). The median follow-up period was 19.1 years (IQR, 10.4 to 20.7).

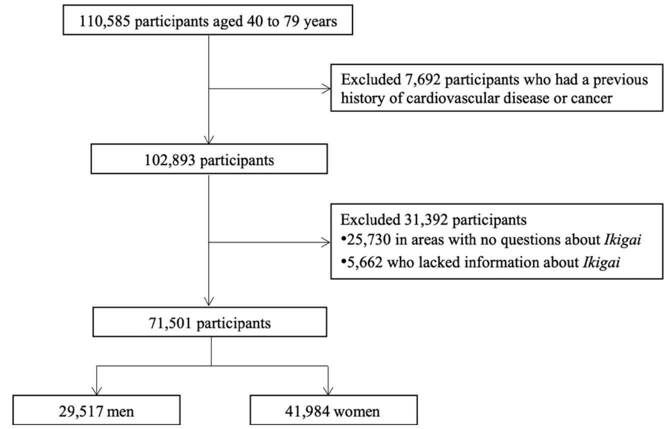

Figure 1 Flowchart for the selection of the study participants.

Baseline measurement

At baseline, we used a self-administered questionnaire to obtain information on age, body mass index (BMI) (calculated by dividing body weight in kg by height m^2), smoking status, alcohol consumption, sleep duration, walking time per day, sports activity time per week, education level, marital status, employment status and psychological conditions such as *Ikigai*, perceived mental stress, sense of life enjoyment and medical history of hypertension and diabetes mellitus. *Ikigai* was assessed using the question 'How much *Ikigai* do you feel in your daily life?' and responses were assessed using a four-point Likert scale: 'low', 'moderate', 'high' and 'very high'. We collapsed 'very high' into 'high' for the analyses, as did previous studies.[25 26] Other psychological conditions were evaluated by single-item questions using four points Likert scale.

Statistical analysis

For each participant, we calculated the person-years of follow-up from the baseline surveys between 1988 and 1990 to the first endpoint of death, moving from the community or the end of 2009. Mortality rates for CVD were estimated according to the perceived levels of *Ikigai* at baseline. We compared sex-specific and age-adjusted mean or prevalence of baseline risk characteristics according to perceived levels of *Ikigai* among participants using the linear regression or Mantel-Haenszel test.

The analysis used a Cox proportional hazards model to calculate sex-specific HRs and 95% CIs of CVD according to perceived levels of *Ikigai* at baseline and the risk of mortality from CVD at follow-up. The adjustment was done for age and then for other potential confounders: BMI (< 18.5, 18.5 to <25.0, 25.0–30.0, 30.0–35.0 and ≥35.0 kg/m^2), smoking status (never, ex-smoker and current smoker), alcohol consumption (never, ex-drinker, 1–20 and ≥20.0 g ethanol per day), sports activity time per week (almost never, 1–2, 3–4 and ≥5 hours/week), walking time per day (almost never, 0.5, 0.6–0.9 and ≥1 hours/day), education levels (<13, 13–15, 16–18 and ≥19 years), marital status (living with a spouse, divorced, bereaved and single), sleep duration per day (<5, 5, 6, 7, 8, 9 and ≥10 hours/day), perceived mental stress (low, moderate, high, very high), sense of life enjoyment (always, sometimes, moderate, never) and medical history of hypertension and diabetes (yes or no). Missing values for these covariates were treated as additional missing categories, and the model contained these dummy variables. Furthermore, the stratified analysis was performed for six categories of employment status; employed, self-employed, part-time workers, homemakers, unemployed and others. Homemakers were regarded as the category of employed because they were primarily women, and many of them were assumed to have motivation for children and housework in Japan. In addition, we conducted a sensitivity analysis to exclude those who died early and those who moved and were censored in the first 5 years of follow-up and the type-specific CVD analysis for total stroke, ischaemic stroke, haemorrhagic stroke, stroke of undetermined type, coronary heart disease, heart failure and other CVDs. To test for linear trends across the *Ikigai* categories for baseline risk characteristics and HRs, ordering variable of *Ikigai* (1: low, 2: moderate, 3: high) was used. Probability values for statistical significance were two-tailed, and a p value <0.05 was regarded as statistically significant. The statistical analyses were carried out using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA).

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting, or dissemination plans of this research.

RESULTS

During a follow-up of 1 160 648 person-years, the deaths of 4680 (men and women: 2393 and 2287) due to total CVD were documented. Other deaths from major CVD types were 2053 (1047 and 1006) total strokes, 716 (398 and 318) ischaemic strokes, 739 (344 and 395) haemorrhagic strokes, 598 (305 and 293) strokes of undetermined type, 975 (550 and 425) coronary heart diseases, 792 (361 and 431) heart failures and 860 (435 and 425) other CVDs.

Table 1 shows the mean values or prevalence of cardiovascular risk factors and health behaviours at baseline according to *Ikigai* level. In both men and women, those with high *Ikigai* tended to have higher levels of the following factors: BMI, self-employed, higher education (≥16 years), current alcohol consumption, never smoking, living with a spouse, sports activity (≥1–2 hours/week), walking time (≥1 hours/day), low perceived mental stress and high life enjoyment. Unlike men, women with high *Ikigai* tended to be employed or part-time workers.

Table 2 shows the sex-specific risk of mortality from total CVD according to the level of *Ikigai*, stratified by employment status. Men who had moderate and high *Ikigai* had a lower risk of mortality from total CVD than those with low *Ikigai*. Multivariable HRs (95% CIs) were 0.80 (0.68 to 0.93) and 0.74 (0.64 to 0.87); P for trend <0.001, respectively. A similar inverse association was observed among unemployed men, multivariable HRs (95% CIs) were 0.74 (0.57 to 0.97) and 0.69 (0.52 to 0.93); P for trend=0.044, respectively. Women who had moderate and high *Ikigai* levels tended to have a lower risk of mortality from total CVD than those with low *Ikigai*. But, tests for trend were not statistically significant: multivariable HRs (95% CI) were 0.87 (0.75 to 1.00) and 0.88 (0.76 to 1.03); P for trend=0.136, respectively. Among unemployed women, those who had moderate and high *Ikigai* had a lower risk of mortality from total CVD than those who had low *Ikigai*; tests for trend were statistically significant: multivariable HRs (95% CI) were 0.78 (0.64 to 0.95) and 0.77 (0.61 to 0.97); P for trend=0.039, respectively. No associations were observed among the unemployed, including part-time workers, self-employed and homemakers for both men and women.

Table 3 shows the sensitivity analysis in which we censored individuals who died and those who moved during the first 5 years of follow-up, having excluded individuals who had an early death. The inverse associations did not differ materially for both men and women.

Table 4 shows the risk of mortality from CVD types according to the perceived levels of *Ikigai* among the unemployed. Unemployed men and women with high *Ikigai* had lower risks of mortality from total stroke, stroke subtypes (ischaemic stroke, haemorrhagic stroke and stroke of determined type), coronary heart disease, heart failure and other CVDs than those with low *Ikigai*. After adjusting for CVD risk factors, the inverse association remained statistically significant for total stroke, stroke of determined type and coronary heart disease.

DISCUSSION

In a large prospective cohort study, higher levels of *Ikigai* were associated with a lower risk of mortality from total CVD among unemployed men and women after adjustment for known cardiovascular risk factors, but such as inverse association was not observed for the employed.

Table 1 Sex-specific mean values and proportions of baseline characteristics according to the perceived levels of *Ikigai*

	Men				Women			
	Low	Moderate	High	P_{Trend}	Low	Moderate	High	P_{Trend}
No. at risk, n (%)	2197 (7.4)	12 240 (41.5)	15 080 (51.1)		3819 (9.1)	20 308 (48.4)	17 857 (42.5)	
Age, years, mean (SD)	57.4 (10.5)	57.2 (10.1)	56.8 (10.2)	<0.001	58.1 (10.8)	57.7 (10.0)	56.8 (9.9)	<0.001
Body mass index, kg/m^2, mean (SD)	22.5 (2.9)	22.5 (2.8)	22.8 (2.8)	<0.001	23.1 (3.5)	22.8 (3.1)	23.1 (3.1)	<0.001
Employment status, n (%)				<0.001				<0.001
Employed	560 (25.5)	4658 (38.1)	5362 (35.6)		385 (10.1)	2714 (13.4)	2550 (14.3)	
Self-employed	423 (19.3)	3860 (31.5)	5669 (37.6)		367 (9.6)	3137 (15.4)	3321 (18.6)	
Part-time worker	24 (1.1)	267 (2.2)	282 (1.9)		290 (7.6)	1987 (9.8)	1779 (10.0)	
Unemployed	436 (19.8)	2262 (18.5)	1802 (11.9)		894 (23.4)	4364 (21.5)	2637 (14.8)	
Homemaker	2 (0.1)	13 (0.1)	9 (0.1)		685 (17.9)	6201 (30.5)	4908 (27.5)	
Other	752 (34.2)	1180 (9.6)	1956 (13)		1198 (31.4)	1905 (9.4)	2662 (14.9)	
Education level, n (%)				<0.001				<0.001
<16 years	714 (48.0)	4465 (39.1)	4079 (30.2)		1329 (49.8)	7686 (40.7)	4826 (30.6)	
16–18 years	556 (37.4)	5252 (46.0)	6515 (48.3)		1128 (42.3)	9580 (50.7)	8874 (56.3)	
≥19 years	217 (14.6)	1712 (15.0)	2891 (21.4)		210 (7.9)	1639 (8.7)	2052 (13.0)	
Alcohol consumption, n (%)				<0.001				<0.001
Never	412 (19.6)	2225 (19.0)	2514 (17.3)		2691 (77.2)	14 305 (76.2)	12 042 (72.0)	
Past	221 (10.5)	694 (5.9)	738 (5.1)		97 (2.8)	294 (1.6)	283 (1.7)	
Current	1468 (69.9)	8814 (75.1)	11 264 (77.6)		697 (20.0)	4173 (22.2)	4408 (26.3)	
Smoking status, n (%)								0.007
Never	413 (19.6)	2322 (19.9)	3153 (21.8)		3053 (91.6)	16 664 (93.5)	14 943 (93.6)	
Past	507 (24.1)	2945 (25.2)	3627 (25.0)		68 (2.0)	253 (1.4)	214 (1.3)	
Current	1186 (56.3)	6416 (54.9)	7708 (53.2)		212 (6.4)	911 (5.1)	814 (5.1)	
Marital status, n (%)				<0.001				<0.001
Living with a spouse	1708 (86.0)	10 358 (93.0)	13 424 (95.4)		2530 (75.4)	15 317 (83.9)	14 081 (84.8)	
Widowed	127 (6.4)	391 (3.5)	368 (2.6)		620 (18.5)	2257 (12.4)	2009 (12.1)	
Divorced	56 (2.8)	182 (1.6)	149 (1.1)		90 (2.7)	417 (2.3)	344 (2.1)	
Single	95 (4.8)	210 (1.9)	134 (1.0)		114 (3.4)	276 (1.5)	176 (1.1)	
Sports activity time, n (%)				<0.001				<0.001
Never	1705 (81.2)	8431 (72.5)	9060 (62.6)		3105 (86.6)	14 951 (79.3)	11 876 (70.6)	
1–2 hours/week	213 (10.1)	1787 (15.4)	2807 (19.4)		272 (7.6)	2343 (12.4)	2803 (16.7)	
3–4 hours/week	108 (5.1)	721 (6.2)	1302 (9.0)		129 (3.6)	851 (4.5)	1188 (7.1)	

Continued

Table 1 Continued

	Men				Women			
	Low	Moderate	High	P_{Trend}	Low	Moderate	High	P_{Trend}
≥5 hours/week	73 (3.5)	687 (5.9)	1307 (9.0)		79 (2.2)	720 (3.8)	956 (5.7)	
Walking time, n (%)				<0.001				<0.0001
Never	294 (18.8)	1354 (11.6)	1307 (9.5)		390 (14.3)	1852 (9.7)	1221 (7.7)	
0.5 hours/day	302 (19.3)	2268 (19.4)	2453 (17.8)		525 (19.3)	3444 (18.0)	2596 (16.4)	
0.5–1 hours/day	271 (17.3)	2339 (20.0)	2788 (20.3)		558 (20.5)	4198 (21.9)	3249 (20.5)	
≥1 hours/day	695 (44.5)	5757 (49.1)	7195 (52.4)		1246 (45.8)	9690 (50.5)	8777 (55.4)	
Sleep duration, hours/day, mean (SD)	7.6 (1.3)	7.5 (1.1)	7.4 (1.1)	0.009	7.2 (1.3)	7.1 (1.1)	7.1 (1.0)	0.008
Perceived mental stress, n (%)				<0.001				<0.001
Low	378 (17.7)	1382 (11.4)	3107 (20.9)		541 (14.6)	2319 (11.6)	4300 (24.4)	
Moderate	1029 (48.1)	8237 (68.2)	8332 (55.9)		1838 (49.8)	13 907 (69.8)	10 169 (57.6)	
High	733 (34.3)	2451 (20.3)	3458 (23.2)		1315 (35.6)	3699 (18.6)	3184 (18.0)	
Sense of life enjoyment, n (%)				<0.001				<0.001
Low	417 (19.2)	399 (3.3)	193 (1.3)		775 (20.7)	686 (3.4)	184 (1.0)	
Moderate	965 (44.4)	9101 (75.0)	5612 (37.5)		1753 (46.7)	15 044 (75.2)	5937 (33.5)	
High	230 (10.6)	2640 (21.7)	8265 (55.2)		315 (8.4)	4288 (21.4)	10 234 (57.8)	
History of hypertension, n (%)	485 (24.7)	2305 (20.5)	2698 (19.2)	0.050	975 (28.0)	4107 (22.3)	3433 (20.8)	0.188
History of diabetes mellitus, n (%)	153 (8.1)	729 (6.6)	895 (6.5)	0.888	197 (5.9)	735 (4.1)	566 (3.5)	0.062

Table 2 Sex-specific, age-adjusted and multivariable HRs and 95% CIs of total cardiovascular mortality according to the perceived levels of *Ikigai*, stratified by employment status

	Men				Women			
	Low	Moderate	High	P_{Trend}	Low	Moderate	High	P_{Trend}
All								
No. at risk	2197	12 240	15 080		3819	20 308	17 857	
No. of person-years	32 824	191 424	244 694		61 744	330 980	298 982	
No. of deaths	251	1007	1135		307	1129	851	
Age-adjusted HR (95% CI)	1.00	0.66 (0.58 to 0.76)	0.57 (0.50 to 0.65)	<0.001	1.00	0.75 (0.66 to 0.86)	0.68 (0.60 to 0.78)	<0.001
Multivariable* HR (95% CI)	1.00	0.80 (0.68 to 0.93)	0.74 (0.64 to 0.87)	<0.001	1.00	0.87 (0.75 to 1.00)	0.88 (0.76 to 1.03)	0.136
Employed								
No. at risk	560	4658	5362		385	2714	2550	
No. of person-years	9479	80 287	92 997		6695	48 860	46 328	
No. of deaths	22	193	192		7	43	44	
Age-adjusted HR (95% CI)	1.00	0.92 (0.59 to 1.44)	0.73 (0.47 to 1.14)	0.051	1.00	0.85 (0.38 to 1.89)	0.89 (0.40 to 1.97)	0.916
Multivariable* HR (95% CI)	1.00	1.02 (0.63 to 1.63)	0.80 (0.49 to 1.31)	0.116	1.00	0.82 (0.35 to 1.95)	1.01 (0.41 to 2.48)	0.679
Self-employed								
No. at risk	423	3860	5669		367	3137	3321	
No. of person-years	6347	61 848	93 546		6025	53 663	56 797	
No. of deaths	35	290	425		9	113	102	
Age-adjusted HR (95% CI)	1.00	0.76 (0.54 to 1.08)	0.71 (0.50 to 1.00)	0.120	1.00	1.14 (0.58 to 2.25)	0.98 (0.50 to 1.94)	0.523
Multivariable* HR (95% CI)	1.00	0.86 (0.60 to 1.24)	0.85 (0.59 to 1.22)	0.682	1.00	1.30 (0.62 to 2.73)	1.29 (0.60 to 2.76)	0.782
Part-time workers								
No. at risk	24	267	282		290	1987	1779	
No. of person-years	336	4037	4344		4941	34 182	30 244	
No. of deaths	2	27	24		7	28	33	
Age-adjusted HR (95% CI)	1.00	0.78 (0.18 to 3.28)	0.51 (0.12 to 2.20)	0.287	1.00	0.55 (0.24 to 1.25)	0.73 (0.32 to 1.65)	0.279
Multivariable* HR (95% CI)	1.00	0.91 (0.17 to 4.76)	0.70 (0.12 to 4.06)	0.762	1.00	0.88 (0.34 to 2.25)	0.79 (0.30 to 2.04)	0.866
Homemakers								
No. at risk	2	13	9		685	6201	4908	
No. of person-years	33	164	137		10 963	100 252	80 823	
No. of deaths	0	0	0		46	266	184	
Age-adjusted HR (95% CI)	–	–	–	–	1.00	0.67 (0.49 to 0.91)	0.57 (0.41 to 0.78)	0.003
Multivariable* HR (95% CI)	–	–	–	–	1.00	0.83 (0.59 to 1.17)	0.84 (0.58 to 1.22)	0.576

Continued

Table 2 Continued

	Men				Women			
	Low	**Moderate**	**High**	**P_{Trend}**	**Low**	**Moderate**	**High**	**P_{Trend}**
Unemployed								
No. at risk	436	2262	1802		894	4364	2637	
No. of person-years	4821	27 595	23 334		11 864	62 898	38 599	
No. of deaths	84	368	250		145	555	306	
Age-adjusted HR (95% CI)	1.00	0.63 (0.50 to 0.80)	0.48 (0.37 to 0.61)	<0.001	1.00	0.70 (0.58 to 0.84)	0.62 (0.51 to 0.76)	<0.001
Multivariable* HR (95% CI)	1.00	0.74 (0.57 to 0.97)	0.69 (0.52 to 0.93)	0.044	1.00	0.78 (0.64 to 0.95)	0.77 (0.61 to 0.97)	0.039
Others								
No. at risk	752	1180	1956		1198	1905	2662	
No. of person-years	11 808	17 493	30 335		21 257	31 124	46 191	
No. of deaths	108	129	244		93	124	182	
Age-adjusted HR (95% CI)	1.00	0.62 (0.48 to 0.80)	0.67 (0.53 to 0.84)	<0.001	1.00	0.81 (0.62 to 1.06)	0.83 (0.65 to 1.06)	0.253
Multivariable* HR (95% CI)	1.00	0.64 (0.47 to 0.87)	0.76 (0.59 to 0.97)	0.016	1.00	0.91 (0.64 to 1.29)	1.00 (0.76 to 1.31)	0.813

*Adjusted for age, body mass index, smoking status, alcohol consumption, sports activity, walking time, sleep duration, education level, employment status, marital status, sense of life enjoyment, perceived mental stress, medical history of hypertension and diabetes mellitus.

Table 3 Sex-specific, multivariable HRs and 95% CIs of total cardiovascular mortality according to the perceived levels of *Ikigai* after exclusion of deaths occurred 1–5 years from the baseline among unemployed persons

	Ikigai			
	Low	**Moderate**	**High**	**P_{Trend}**
Men				
At risk	436	2262	1802	
Person-years	4821	27 595	23 334	
No. of deaths	84	368	250	
Multivariable* HR	1.00	0.74 (0.57 to 0.97)	0.69 (0.52 to 0.93)	0.044
	79	358	243	
Deaths within 1 year exclude*	1.00	0.74 (0.56 to 0.97)	0.68 (0.51 to 0.92)	0.044
	73	343	232	
Deaths within 2 years exclude*	1.00	0.77 (0.58 to 1.02)	0.71 (0.52 to 0.96)	0.087
	67	318	223	
Deaths within 3 years exclude*	1.00	0.75 (0.56 to 1.01)	0.71 (0.52 to 0.98)	0.104
	60	299	210	
Deaths within 4 years exclude*	1.00	0.78 (0.57 to 1.06)	0.72 (0.52 to 1.01)	0.157
	56	282	201	
Deaths within 5 years exclude*	1.00	0.75 (0.55 to 1.04)	0.69 (0.49 to 0.98)	0.115
Women				
No. at risk	894	4364	2637	
No. of person-years	11 864	62 898	38 599	
No. of deaths	145	555	306	
Multivariable* HR	1.00	0.78 (0.64 to 0.95)	0.77 (0.61 to 0.97)	0.039
	138	540	299	
Deaths within 1 year excluded*	1.00	0.78 (0.64 to 0.96)	0.78 (0.62 to 0.98)	0.056
	134	526	290	
Deaths within 2 years excluded*	1.00	0.79 (0.64 to 0.97)	0.78 (0.61 to 0.98)	0.061
	125	498	281	
Deaths within 3 years excluded*	1.00	0.77 (0.62 to 0.96)	0.78 (0.61 to 1.00)	0.057
	113	480	273	
Deaths within 4 years excluded*	1.00	0.81 (0.65 to 1.02)	0.83 (0.65 to 1.08)	0.193
	112	462	267	
Deaths within 5 years excluded*	1.00	0.78 (0.62 to 0.97)	0.80 (0.62 to 1.04)	0.092

*Adjusted for age, body mass index, smoking status, alcohol consumption, sports activity, walking time, sleep duration, education level, employment status, marital status, sense of life enjoyment, perceived mental stress, medical history of hypertension and diabetes mellitus.
†

The lower risk of CVD mortality among the unemployed was observed even after excluding early deaths within 5 years from the baseline survey. Furthermore, the risk reduction was evident for total stroke and coronary heart disease among the unemployed people.

The underlying biological mechanisms for the potential preventive effect of *Ikigai* on mortality from CVD remained unclear, but some reasons have been addressed. Elevated levels of inflammatory markers such as C reactive protein and interleukin-6 were associated with an increased CVD risk.[27–29] A previous study using data from a 10-year panel survey of 985 adults aged 25–74 years residing in the USA showed that people with a higher purpose in life had lower physiological function scores, calculated by summarising biomarkers such as resting blood pressure, heart rate variability, low-density lipoprotein cholesterol, glycosylated haemoglobin, plasma C reactive protein, interleukin-6, urinary measures of epinephrine/norepinephrine and cortisol levels.[30] Another study of 135 older women aged 61–91 years found that those with higher scores of purpose in life had lower levels of the soluble IL-6 receptor, an inflammatory marker for stroke, coronary heart disease as well as rheumatoid arthritis and Alzheimer's disease.[31]

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Table 4 Age-adjusted and sex-adjusted and multivariable HRs and 95% CIs of mortality from type-specific cardiovascular diseases according to the perceived levels of *Ikigai* among unemployed persons

		Ikigai			
		Low	Moderate	High	P_{Trend}
Total stroke	No. at risk	1330	6626	4439	
	No. of person-years	16 684	90 493	61 933	
	No. of deaths	107	375	242	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.58 (0.47 to 0.72)	0.51 (0.41 to 0.65)	<0.001
	Multivariable* HR (95% CI)	1.00	0.72 (0.57 to 0.91)	0.74 (0.56 to 0.96)	0.022
Ischaemic stroke	No. of deaths	37	157	91	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.70 (0.49 to 1.00)	0.54 (0.37 to 0.80)	0.007
	Multivariable* HR (95% CI)	1.00	0.82 (0.56 to 1.20)	0.80 (0.51 to 1.24)	0.555
Haemorrhagic stroke	No. of deaths	30	95	67	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.54 (0.36 to 0.82)	0.54 (0.35 to 0.83)	0.008
	Multivariable* HR (95% CI)	1.00	0.74 (0.47 to 1.19)	0.84 (0.49 to 1.42)	0.425
Stroke of undetermined type	No. of deaths	40	123	84	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.51 (0.36 to 0.73)	0.47 (0.32 to 0.69)	<0.001
	Multivariable* HR (95% CI)	1.00	0.61 (0.41 to 0.90)	0.61 (0.39 to 0.96)	0.041
Coronary heart disease	No. of deaths	43	196	99	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.75 (0.54 to 1.05)	0.51 (0.36 to 0.74)	<0.001
	Multivariable* HR (95% CI)	1.00	0.77 (0.54 to 1.10)	0.64 (0.43 to 0.97)	0.103
Heart failure	No. of deaths	43	187	120	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.73 (0.52 to 1.01)	0.65 (0.46 to 0.92)	0.055
	Multivariable* HR (95% CI)	1.00	0.90 (0.63 to 1.30)	1.01 (0.67 to 1.52)	0.663
Other CVDs	No. of deaths	36	165	95	
	Age-adjusted, sex-adjusted HR (95% CI)	1.00	0.75 (0.52 to 1.08)	0.60 (0.40 to 0.87)	0.023
	Multivariable* HR (95% CI)	1.00	0.75 (0.51 to 1.11)	0.64 (0.42 to 1.00)	0.144

*Adjusted for age, sex, body mass index, smoking status, alcohol consumption, sports activity, walking time, sleep duration, education level, employment status, marital status, sense of life enjoyment, perceived mental stress, medical history of hypertension and diabetes mellitus.
CVD, cardiovascular disease.

Two other prospective cohort studies using 9.1-year follow-up data for 941 persons and 6-year follow-up data for 2478 persons showed that the risk reductions associated with positive psychological factors in all-cause mortality and stroke incidence were stronger in men than in women.[32 33] A previous report of the JACC study with a 12.5-year follow-up showed that men with higher *Ikigai* had a reduced risk of CVD mortality but not women.[34] We observed a similar inverse association of CVD mortality risk in the present study and extended the evidence that the inverse association between *Ikigai* and CVD mortality risk was confined to unemployed men and women.

The present study has several strengths compared with previous studies. First, a population-based cohort study with a large sample size and a more extended follow-up period allowed us to assess the risk of cardiovascular mortality according to the perceived levels of *Ikigai*, stratified by employment status. Second, we adjusted for many confounding factors including lifestyle habits, social and psychological factors and medical histories such as hypertension and diabetes mellitus. There were some limitations to our study. First, psychological factors such as *Ikigai* were evaluated by a self-administered single-item questionnaire. It has been noted that *Ikigai* encompasses not only eudaimonic well-being, that is, well-being that pertains to internal virtue and pursuing human capacity,[35] but also aspects of hedonic well-being characterised by pleasure and satisfaction not necessarily resulting from a virtuous activity.[36] Unemployed persons with *Ikigai* were possibly likely to have available eudaimonic or hedonic well-being in their daily lives. However, the present study did not provide information on the details of *Ikigai*. Second, the presence of illness and preclinical conditions may have influenced *Ikigai* at baseline, which could lead to reverse causality. Therefore, we excluded histories of CVD and cancer and also conducted a sensitivity analysis in which individuals who died or moved during the first 5 years of follow-up were censored and found that the inverse association between *Ikigai* and the risk of CVD mortality remained unchanged. Lastly, although we adjusted for numerous potential confounders, some unmeasured confounders, such as the usage of medical services, may still be present. A previous study using a national panel study of 7168 US adults showed that having a purpose in life was associated with a higher likelihood of using healthcare services such as cholesterol tests, colonoscopies, mammogram/X-ray, pap smear and prostate examinations.[37]

CONCLUSION

We found that higher levels of *Ikigai* were associated with a lower risk of CVD mortality, specifically for unemployed men and women. Having *Ikigai* might be useful for the risk reduction of CVD mortality among the unemployed.

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Contributors HI and AT conceived and designed the study. JM and KS drafted the plan for the data analyses. JM and TK conducted data analysis. SI and TK provided statistical expertise and interpreted the data. JM drafted the manuscript. HI and KS analysed and interpreted the data, and critically revised the manuscript. JM, KS and HI had primary responsibility for final content. All authors were involved in the interpretation of the results and revision of the manuscript and approved the final version of the manuscripts. JM, KS and HI are guarantors.

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