Ikigai and subsequent health and wellbeing among Japanese older adults: Longitudinal outcome-wide analysis

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Summary

Background Having a purpose in life has been linked to improved health and wellbeing; however, it remains unknown whether having "*Ikigai*"—a related but broader concept in Japan—is also beneficial for various physical and psychosocial outcomes.

Methods Using data from a nationwide longitudinal study of Japanese older adults aged ≥65 years, we examined the associations between having *Ikigai* in 2013 and a wide range of subsequent outcomes assessed in 2016 across two databases (n = 6,441 and n = 8,041), including dimensions of physical health, health behavior, psychological distress, social wellbeing, subjective wellbeing, and pro-social/altruistic behaviors. We adjusted for sociodemographic characteristics and the outcome values (whenever data were available) in the prior wave (2010).

Findings Having *Ikigai* (vs. not having *Ikigai*) was associated with a 31% lower risk of developing functional disability [95% confidence interval (CI) for risk ratio: 0.58, 0.82] and 36% lower risk of developing dementia [95% CI for risk ratio: 0.48, 0.86] during the three-year follow-up. Having *Ikigai* was associated with decreased depressive symptoms and hopelessness as well as higher happiness, life satisfaction, instrumental activity of daily living, and certain social outcomes (e.g., more frequent participation in hobby clubs). Some of these associations were stronger for men than women, and among individuals with high socioeconomic status (p-values for effect measure modification < 001).

Interpretation Having *Ikigai* may promote health and wellbeing outcomes among Japanese older adults, but particularly men and individuals with high socioeconomic status.

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Keywords: Ikigai; Purpose in life; Aging; Wellbeing; Asia

Introduction

Public health and epidemiology have focused on reducing disease risk factors (e.g., smoking) to promote population health.[1] In contrast, growing evidence suggests that cultivating positive psychological assets—factors related to positive psychosocial and spiritual aspects of

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Research in context

Evidence before this study

While there is a wealth of evidence linking having a purpose in life to longevity and improved health/wellbeing of older adults, little is known about whether having *Ikigai*—a related but not identical psychological concept—is likewise beneficial for healthy aging. We searched PubMed using the search term "*Ikigai*", "health", "well-being", with no language restrictions, from Jan 1979 to Jan 2021. We found only a few studies that investigated the longitudinal association between *Ikigai*, health, and wellbeing. These studies examined a narrow range of health/wellbeing outcomes and lacked rigorous adjustment for confounding and reverse causation.

Added value of this study

To our knowledge, this is the first study to holistically evaluate associations between *Ikigai* and a wide range of subsequent health and wellbeing, including dimensions of physical health, health behavior, psychological distress, social wellbeing, subjective wellbeing, and prosocial/altruistic behaviors. We leveraged a large, nationwide, longitudinal cohort study of Japanese older adults and adjusted for a rich set of potential confounders, including pre-baseline outcome values to address reverse causation. This study demonstrated that having *Ikigai* was longitudinally associated with some favorable physical health outcomes (lower risk of developing functional disabilities and dementia), reduced psychological distress (depressive symptoms and hopelessness), and improved subjective wellbeing (happiness and life satisfaction). Moreover, our study revealed a bidirectional association between *Ikigai* and psychological distress. Some of these associations were stronger for men and individuals with high socioeconomic status.

Implication of all the available evidence

Although more research is needed to understand why *Ikigai* appeared less beneficial for some outcomes and among women and individuals with low SES, *Ikigai* may be a promising modifiable positive psychological asset, which can supplement the current public health efforts to *reduce* risk factors to promote health and wellbeing.

life—can also contribute to improved health and wellbeing.[2] One potentially modifiable psychological asset is purpose in life, which is the extent to which individuals perceive their lives as having aims that generate and prioritize their pursuits and actions.[3,4] In studies of the US-based populations, higher levels of purpose in life have been linked to greater subjective wellbeing (e.g., life satisfaction), healthier behaviors, and reduced morbidity and mortality risk.[5,6]

Ikigai, broadly defined as "what makes life worth living," is a well-accepted psychological concept in the Japanese culture.[7] In efforts aimed at promoting longer and healthier lives, the Japanese government recently decided that increasing *Ikigai* among older adults is a policy priority.[8] Although *Ikigai* and purpose in life share many features, *Ikigai* is broader: while purpose in life refers to one aspect of eudaimonic wellbeing (i.e., wellbeing that pertains to internal virtue and pursuing human capacity),[3] *Ikigai* is characterized not only by purpose in life but also by other aspects of eudaimonic wellbeing (e.g., personal growth) as well as features of hedonic wellbeing (i.e., pleasure and satisfaction which do not necessarily result from virtuous activities).[2,9,10] For example, some people may derive their *Ikigai* through activities that promote purpose in life such as volunteering, others may cultivate *Ikigai* by fulfilling one's own need (e.g., reading books to satisfy curiosity) or simply indulging in pleasure (e.g., enjoying drinks with peers). Despite the nuanced conceptual differences between *Ikigai* and purpose in life, most available longitudinal evidence focuses predominantly on purpose in life, rather than *Ikigai*, in relation to future health and wellbeing. Emerging evidence from *Ikigai* studies suggest that having *Ikigai* is associated with a reduced risk of cardiovascular disease, mortality, and functional disability.[11–18]

These past studies provided important insights about the potential health benefits of *Ikigai*; however, three methodological limitations remain unaddressed. First, several of these studies did not include important potential confounders (e.g., depressive symptoms). Second, even though these studies harnessed longitudinal data, they inadequately accounted for pre-baseline health conditions, so that the potential for reverse causation (i.e., better health and wellbeing leading to greater *Ikigai*, not vice versa) could not be precluded. Lastly, although health is a multidimensional construct (often defined as "a state of complete physical, psychological, and social wellbeing" rather than the mere absence of diseases), the existing evidence on the health benefits of *Ikigai* is restricted to physical health outcomes.[19,20] Assessing a more comprehensive set of outcomes simultaneously can facilitate comparisons of the directions and magnitudes of the *Ikigai*-health association across outcomes and provide a more holistic picture (e.g., *Ikigai* may be beneficial for some outcomes but have a detrimental impact on others). Such analytic approach can also prevent selective reporting of study findings and publication bias.[1,21]

To address these gaps, we applied an outcome-wide approach to examine the prospective associations of *Ikigai* with multiple health and wellbeing outcomes using the nationwide longitudinal sample of Japanese older adults.[20,22] To reduce the concerns about unobserved confounding and reverse causation, we leveraged the

rich panel structure of the data and rigorously adjusted for pre-existing health conditions such as depression.

Method

Study sample

We used data from the Japan Gerontological Evaluation Study (JAGES), a nationwide longitudinal survey of physically and cognitively independent community-dwelling older adults aged ≥ 65 years in Japan.[23] In 2010, the JAGES was established and collected data on sociodemographic factors, health conditions, and well-being from 78,873 individuals in 19 municipalities in Japan (response rate: 69.3%). In 2013 (our study's baseline wave), the JAGES conducted the follow-up survey (n = 54,283 individuals; follow-up rate = 68.8%) and randomly selected 20% of the participants to fill out a questionnaire which contained an *Ikigai* assessment (n = 10,867). We obtained two analytic samples by linking these 10,867 individuals either to the second follow-up wave of the main survey in 2016 (n = 6,441; follow-up rate = 59.3%) or to the national long-term care insurance database containing information on the onset of all-cause mortality, functional disability, and dementia through 2016 (i.e., n = 8,041; follow-up rate = 74.0%). We used the two different analytic samples to increase our sample size. Participation in the 2016 follow-up wave was not necessary for the analysis of the outcomes from the long-term care insurance database. See Figure 1 for the flow chart.

Measures

Ikigai. Participants reported whether they had *Ikigai* in their life at the time of the survey in 2013. The survey question asked, "Do you have *Ikigai*?" with a binary response option (yes or no).

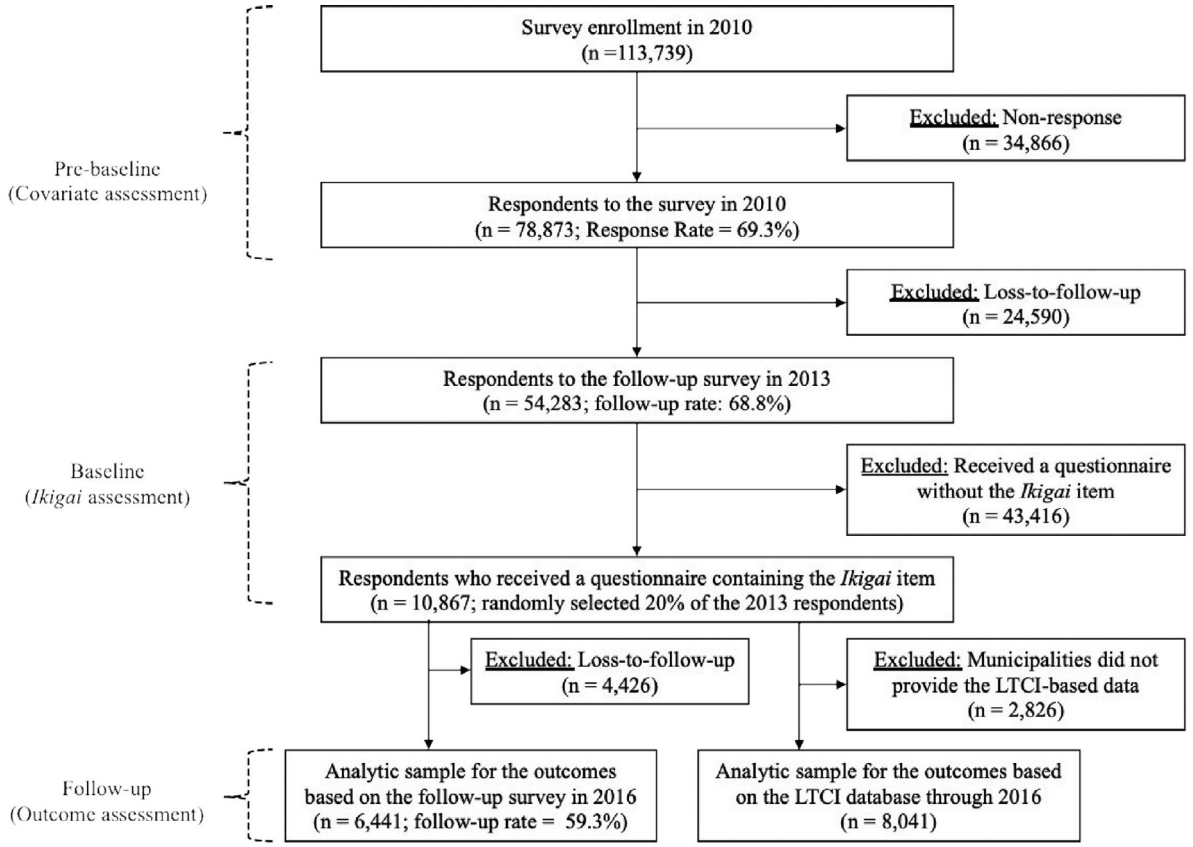
Outcomes. We examined 30 health and wellbeing outcomes in 2016, including physical health (all-cause mortality, functional disability,[22,24] dementia,[25] no remaining natural teeth, self-rated health, flu infection in the past year, pneumonia infection in the past year, and instrumental daily activities of living [IADL]),[26] health behaviors (current smoking, body mass index [BMI], sedentary lifestyle, insomnia, flu shot in the past year, health check-up in the past year), psychological distress (depressive symptoms [27] and hopelessness), social wellbeing (participation in a hobby group, sports group, or senior citizens club, frequency of meeting friends, number of friends seen per month, emotional social support, and care social support), subjective well-being (happiness, and life satisfaction), and pro-social behaviors (volunteering and sharing skills and experiences). We chose these outcomes based on VanderWeele's multidimensional concept of human flourishing as a framework.[28] Although other theorizing and measures of multidimensional well-being exist, we chose this framework as it covers physical health in addition to a number of domains shared by the various frameworks.[29–32] Table S1 provides further details about each outcome measurement.

Covariates. All pre-baseline covariates were drawn from the 2010 survey three years before the *Ikigai* assessment. These covariates included age, gender, marital status, living alone, education, job, equivalized household income, the number of self-reported health conditions, and the number of major life events in the past year. To reduce the possibility of reverse causation (i.e., health and wellbeing affecting having *Ikigai*), we also controlled for prior values of all outcomes from the 2010 survey, except for the following outcomes because the data were not available: sedentary lifestyle, flu shot in the past year, infection in the past year (flu, or pneumonia), insomnia, happiness, and sharing skills and experiences.

Statistical analysis

We used a longitudinal outcome-wide analytic approach, which enables a holistic assessment of the impact of a single exposure on a wide range of outcomes and has several other methodological advantages (e.g., less susceptible to "p-hacking"—deliberately or unconsciously changing analytic approaches to obtain results with $p < 0.05$—and publication bias).[20,21] We fitted a separate regression model for each outcome and repeated the analysis of individual outcomes one by one. To estimate the associations between *Ikigai* and each outcome adjusting for the pre-baseline covariates and outcomes in the pre-baseline wave, we used the doubly-robust targeted maximum likelihood estimation.[33] This approach estimates both the exposure (propensity score) model and outcome model and, under the assumption of no unmeasured confounding, yields unbiased estimates for the average treatment effects if either of the two models is consistently estimated. Hence, the approach improves statistical estimation, not causal identification, and is more robust to model misspecification. We estimated risk ratios (RRs) for the binary outcomes. All continuous outcomes were standardized (mean = 0, standard deviation = 1), so the effect estimates can be interpreted as a standard deviation change in the outcome variable. We used Bonferroni correction to account for multiple testing.

We conducted three additional analyses. First, we examined potential antecedents of *Ikigai*. We used a modified Poisson regression with robust standard errors to estimate the RR for the association between each of



LTCI: Long-term care insurance

Figure 1. Flow of Samples Selection (n=6,441 for the Outcomes Based on the Follow-up Survey in 2016 and n=8,041 for the Outcomes Based on the Long -term Care Insurence Database). LTCI: Long-term care insurence.

the pre-baseline covariates and *Ikigai* in 2013, simultaneously controlling for all other covariates.[34] Second, to evaluate the robustness of our effect estimates to unmeasured confounding, we calculated E-values for each *Ikigai*-outcome association.[35] E-values quantify the minimum strength of association on the RR scale that an unmeasured confounder would need to have with both the exposure and outcome, above and beyond the adjusted covariates, to explain away the observed association. Third, given emerging evidence suggesting potential heterogeneity in *Ikigai*-health associations, we performed subgroup analyses for the outcome-wide associations and antecedents of *Ikigai* to examine whether the associations differ by socioeconomic status (SES) and gender.[36–38] We defined binary SES as reporting both low educational attainment (< 10 years of schooling) and low equivalized household income (< 2 million yen/year: approximately 18,400 USD as of March 1, 2021) in the 2010 wave, which follows benchmarks set by previous studies in Japan.[39,40] We formally tested for effect measure modification by comparing the subgroup-specific estimates, on both additive (difference in standardized differences for continuous outcome and difference in risk differences for binary outcomes) and multiplicative scales (ratio of RRs for binary outcomes).

We used multiple imputation by chained equations to impute missing data on all variables, using the *mice* R package.[41] After generating five imputed datasets, we performed the analyses described above using each imputed dataset and combined the results across imputations (more details on missing data and our imputation approach is available in Table S2 and Appendix). All analyses were conducted in R, version 3.6.0.

Role of the funding source

The founders on the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

Table 1 summarizes the pre-baseline characteristics of the study sample linked to the 2016 wave (n = 6,411) according to *Ikigai* status in 2013. Compared to those without *Ikigai* (n = 776), people with *Ikigai* (n = 5,205) tended to be married, highly educated, and currently working. Having *Ikigai* was also associated with better pre-baseline levels of all health and wellbeing except for body mass index. The same trends were found for the pre-baseline characteristics of the study sample linked to the national long-term care insurance record (n = 8,041; Table S3).

Table 2 shows the estimated standardized differences in the continuous outcomes and RRs for binary outcomes comparing those with versus without *Ikigai*, controlling for all aforementioned covariates. Having *Ikigai* was strongly associated with lower risk of developing functional disabilities, higher IADL, fewer depressive symptoms, lower risk of having a sense of hopelessness, more frequent participation in hobby clubs, higher chance of reporting life satisfaction, and more frequent sharing of skills and experiences with others. These associations remained below the $p < 0.05$ threshold even after accounting for multiple testing via Bonferroni correction. We also found modest evidence for the associations between having *Ikigai* and lower risk of dementia, sedentary lifestyle, and insomnia, more frequent participation in sport clubs, and higher likelihood of having emotional social support; however, these additional associations were not below the $p < 0.05$ threshold after Bonferroni correction for multiple testing.

While the results were generally similar across levels of SES (Table S4) for most outcomes (e.g., all-cause mortality), there was some evidence of effect measure modification such that *Ikigai* is more strongly associated with better physical health outcomes in the high SES group. In subgroup analysis by gender (Table S5), we observed associations between *Ikigai* and physical health outcomes only among men. The association between *Ikigai* and all-cause mortality was modest in the whole sample; but the evidence for an association was stronger among men, although this did not reach the $p < 05$ threshold after Bonferroni correction. We also found evidence of effect measure modification for outcomes in other domains (e.g., psychological distress) and evidence for associations with greater wellbeing tended to be stronger among men.

Of the covariates assessed in 2010, greater depressive symptoms, hopelessness, and female gender were strong predictors of not having *Ikigai* in 2013 (Table 3). There was modest evidence that having emotional social support, experiencing fewer major life events in the past year, greater IADL, and not being a current smoker (all assessed in 2010) were predictive of having *Ikigai* in 2013; but all other measured covariates in 2010 were not antecedents of *Ikigai* in 2013. We observed similar results when the analysis for antecedents of *Ikigai* was stratified by SES (Table S6) and by gender (Table S7).

The calculated E-values (Table 4) suggest that some of the observed associations of having *Ikigai* with subsequent health and wellbeing outcomes were moderately robust to an unmeasured confounder. For example, to explain away the association between having *Ikigai* and the risk of developing functional disability during the follow-up, an unmeasured confounder associated with both *Ikigai* and the functional disability by the RR of 2.26—above and beyond the adjusted covariates—could suffice, but weaker joint unmeasured confounding associations could not; to shift the confidence interval to include the null value, unmeasured confounding

Pre-baseline characteristics	Overall	*Ikigai* in 2013[a]		p-value[b]
	n = 6,411	No n = 776	Yes n = 5,205	
Sociodemographic factors				
Age, mean (SD)	71.9 (5.1)	71.8 (4.9)	71.8 (5.0)	0.923
Gender, n (%)				<0.001
Men	2,931 (46%)	309 (40%)	2,460 (47%)	
Women	3,510 (54%)	467 (60%)	2,745 (53%)	
Marital status, n (%)				<0.001
Married	4,771 (76%)	535 (71%)	3,940 (77%)	
Widowed	1,168 (19%)	145 (19%)	903 (18%)	
Divorced	187 (3.0%)	32 (4.3%)	141 (2.8%)	
Single	115 (1.8%)	27 (3.6%)	79 (1.6%)	
Other	35 (0.6%)	12 (1.6%)	23 (0.5%)	
Living alone, n (%)	703 (11%)	116 (15%)	514 (10%)	<0.001
Education, n (%)				<0.001
<6 years	87 (1.4%)	16 (2.1%)	62 (1.2%)	
6-9 years	2,691 (43%)	409 (54%)	2,041 (40%)	
10-12 years	2,271 (36%)	230 (31%)	1,905 (37%)	
≥13 years	1,204 (19%)	93 (12%)	1,057 (21%)	
Other	28 (0.4%)	4 (0.5%)	22 (0.4%)	
Job, n (%)				0.006
Working	1,553 (27%)	154 (23%)	1,318 (28%)	
Retired	3,521 (62%)	438 (64%)	2,868 (61%)	
Never worked	644 (11%)	88 (13%)	499 (11%)	
Equivalized household income (10,000 yen), mean (SD)	151 (93)	128 (86)	156 (94)	<0.001
Number of life events in the past year, mean (SD)	0.82 (0.92)	0.88 (0.95)	0.81 (0.91)	0.071
Physical health				
Number of health conditions, mean (SD)	1.44 (1.38)	1.71 (1.53)	1.39 (1.35)	<0.001
No remaining natural teeth, n (%)	620 (9.9%)	106 (14%)	449 (8.9%)	<0.001
Good self-rated health, n (%)	5,489 (87%)	558 (74%)	4,564 (89%)	<0.001
Instrumental Activity of Daily Living, mean (SD)	11.9 (1.53)	11.2 (1.92)	12.0 (1.42)	<0.001
Health behaviors				
Current smoker, n (%)	593 (10%)	101 (14%)	457 (9.6%)	<0.001
Body mass index, mean (SD)	23.1 (5.09)	22.9 (3.20)	23.1 (4.66)	0.3
Participating health check-up in the past year, n (%)	4,191 (67%)	440 (59%)	3,485 (69%)	<0.001
Psychological distress				
Depressive symptoms, mean (SD)	2.97 (3.00)	6.43 (3.70)	2.43 (2.49)	<0.001
Hopelessness, n (%)	1,031 (17%)	375 (51%)	565 (11%)	<0.001
Social wellbeing				
Frequency of participation in hobby clubs, mean (SD)	2.40 (1.57)	1.96 (1.47)	2.48 (1.58)	<0.001
Frequency of participation in sport clubs, mean (SD)	2.00 (1.58)	1.65 (1.33)	2.07 (1.61)	<0.001
Frequency of participation in senior clubs, mean (SD)	1.49 (1.01)	1.38 (0.88)	1.50 (1.02)	0.004
Frequency of meeting friends, mean (SD)	3.85 (1.47)	3.41 (1.49)	3.91 (1.46)	<0.001
Number of friends I met last month, mean (SD)	2.27 (1.25)	2.74 (1.31)	2.19 (1.23)	<0.001
Emotional social support, n (%)	5,807 (95%)	652 (88%)	4,764 (96%)	<0.001
Care social support, n (%)	5,864 (96%)	659 (89%)	4,810 (97%)	<0.001
Subjective wellbeing				
Life satisfaction, n (%)	5,235 (83%)	422 (56%)	4,473 (87%)	<0.001
Pro-social/altruistic behaviors				
Frequency of volunteering, mean (SD)	1.43 (0.98)	1.26 (0.78)	1.46 (1.00)	<0.001

***Table 1*: Pre-baseline Demographic Characteristics in 2010 Stratified by *Ikigai* Among the Analytic Sample for the Analysis of the Outcomes from the JAGES Survey (n = 6,441).**

[a] Sample sizes for the *Ikigai* strata in this table do not add up to the overall sample size (n = 6,441) because of missing in the *Ikigai* variable.

[b] P-values were calculated using Pearson's Chi-square test for categorical variables and Wilcoxson rank sum test for continuous variables.

Outcome	β	RR	95%CI		P-value	Sig.[b]
			Lower	Upper		
Physical health						
All-cause mortality[c]		0.85	0.60	1.19	0.328	N.S.
Functional Disability (Any levels)[c]		0.69	0.58	0.82	<0.001	***
Functional Disability (Level 1 or greater)[c]		0.67	0.54	0.83	<0.001	***
Functional Disability (Level 2 or greater)[c]		0.71	0.53	0.96	0.027	*
Functional Disability (Need support)[c]		0.70	0.54	0.92	0.011	*
Dementia[c]		0.64	0.48	0.85	0.002	**
No remaining natural teeth		0.92	0.74	1.15	0.464	N.S.
Good self-rated health		1.05	1.00	1.10	0.070	N.S.
Instrumental Activity of Daily Living	0.19		0.10	0.28	<0.001	***
Health behaviors						
Current smoker		1.10	0.82	1.48	0.519	N.S.
Body mass index	0.01		-0.05	0.07	0.766	N.S.
Sedentary lifestyle		0.62	0.42	0.92	0.018	*
Flu shot in the past year		1.00	0.93	1.07	0.902	N.S.
Infection in the past year (flu)		1.42	0.66	3.06	0.362	N.S.
Infection in the past year (pneumonia)		1.59	0.51	5.03	0.423	N.S.
Participating health check-up in the past year		1.03	0.94	1.13	0.468	N.S.
Insomnia[d]		0.55	0.34	0.89	0.014	*
Psychological distress						
Depressive symptoms	-0.58		-0.68	-0.48	<0.001	***
Hopelessness		0.43	0.37	0.51	<0.001	***
Social wellbeing						
Frequency of participation in hobby clubs	0.19		0.09	0.28	<0.001	***
Frequency of participation in sport clubs	0.09		0.00	0.17	0.047	*
Frequency of participation in senior clubs	0.03		-0.09	0.14	0.645	N.S.
Frequency of meeting friends	0.07		-0.02	0.15	0.114	N.S.
Number of friends I met last month	0.08		0.00	0.17	0.050	N.S.
Emotional social support		1.03	1.00	1.06	0.033	*
Care social support		1.03	0.98	1.02	0.742	N.S.
Subjective wellbeing						
Happiness	0.43		0.33	0.52	<0.001	***
Life satisfaction		1.14	1.09	1.21	<0.001	***
Pro-social/altruistic behaviors						
Frequency of volunteering	0.07		-0.04	0.17	0.201	N.S.
Frequency of sharing skills and experiences	0.17		0.08	0.26	<0.001	***

***Table 2*: Associations between *Ikigai* and subsequent health and well-being, Japan gerontological evaluation study (n = 6,441)[a].**
CI, confidence interval; Sig., significance; N.S., not significant; RR, risk ratio; *β*, standardized difference.

[a] We estimated standardized differences for the continuous outcomes and risk ratios for the binary outcomes, using the doubly robust targeted maximum likelihood estimation. We adjusted for pre-baseline covariates (age, gender, marital status, living alone, education, job, equivalized household income, the number of self-reported health conditions, and the number of major life events in the past year) as well as prior levels of outcomes wherever data were available to address reverse causation.

[b] *p<0.05 before Bonferroni correction; ** p<0.01 before Bonferroni correction; *** p<0.05 after Bonferroni correction (the p-value cutoff for Bonferroni correction is p = 0.05/30 outcomes = p <0.0017).

[c] The analytic sample size was n = 8,951 for the following outcomes: all-cause mortality, functional disabilities, and dementia.

[d] Items for insomnia were available only in the submodule questionnaire in 2016 that was distributed to randomly selected 826 individuals.

associations of 1.74-fold each could suffice, but weaker confounding could not.

Discussion

In this nationwide longitudinal study of Japanese older adults, our main findings are four-fold. First, *Ikigai* was associated with some favorable physical health outcomes such as lower risk of developing functional disabilities, particularly among men and those from higher SES backgrounds. Second, *Ikigai* was also associated with reduced psychological distress (depressive symptoms and hopelessness) and improved subjective wellbeing (happiness and life satisfaction), though

Predictors in 2010	RR[a]	95% CI		P-value	Sig.[b]
		Lower	Upper		
Sociodemographic factors					
Age	1.01	0.99	1.02	0.366	N.S.
Women (vs. Men)	0.95	0.93	0.98	<0.001	***
Marital status (vs. Married)					
Widowed	1.01	0.98	1.04	0.496	N.S.
Divorced	1.06	0.99	1.13	0.086	N.S.
Single	0.98	0.88	1.09	0.754	N.S.
Other	0.85	0.70	1.04	0.119	N.S.
Living alone	0.97	0.93	1.02	0.219	N.S.
Education (vs. <6 years)					
6-9 years	0.98	0.87	1.11	0.742	N.S.
10-12 years	1.01	0.89	1.15	0.864	N.S.
≥13 years	1.01	0.89	1.14	0.894	N.S.
Other	0.98	0.81	1.18	0.795	N.S.
Job (vs. Never worked)					
Retired	1.00	0.97	1.04	1.000	N.S.
Working	1.01	0.97	1.06	0.520	N.S.
Equivalized household income (10,000 yen)	1.00	0.99	1.01	0.424	N.S.
Number of major life events in the past year	1.01	1.00	1.02	0.033	*
Physical health					
Number of health conditions	1.01	0.99	1.02	0.277	N.S.
No teeth	0.98	0.95	1.02	0.350	N.S.
Good self-rated health	1.00	0.97	1.05	0.831	N.S.
Instrumental Activity of Daily Living	1.02	1.00	1.04	0.039	*
Health behaviors					
Current smoker	0.96	0.93	1.00	0.027	*
Body mass index	1.00	0.99	1.02	0.955	N.S.
Participating health check-up in the past year	1.01	0.99	1.03	0.516	N.S.
Psychological distress					
Depressive symptoms	0.86	0.84	0.89	<0.001	***
Hopelessness	0.88	0.84	0.93	<0.001	***
Social wellbeing					
Frequency of participation in hobby clubs	1.00	0.99	1.02	0.454	N.S.
Frequency of participation in sport clubs	1.00	0.98	1.01	0.556	N.S.
Frequency of participation in senior clubs	1.01	1.00	1.02	0.206	N.S.
Frequency of meeting friends	1.00	0.99	1.01	0.881	N.S.
Number of friends I met last month	1.01	1.00	1.02	0.187	N.S.
Emotional social support	1.10	1.03	1.19	0.008	**
Care social support	1.09	1.00	1.19	0.051	N.S.
Subjective wellbeing					
Life satisfaction	1.04	1.00	1.09	0.083	N.S.
Pro-social/altruistic behaviors					
Frequency of volunteering	1.00	0.98	1.01	0.387	N.S.

***Table 3*: Antecedents of *Ikigai* in 2013, Japan gerontological evaluation study (n = 6,441).**
CI, confidence interval; Sig., significance; N.S., not significant; RR, risk ratio.
[a] We used a modified Poisson regression with robust standard errors was used to estimate the prevalence ratio for the association between each of the predictors in 2010 and *Ikigai* in 2013, simultaneously controlling for all other covariates.
[b] *p<0.05 before Bonferroni correction; ** p<0.01 before Bonferroni correction; *** p<0.05 after Bonferroni correction (the p-value cutoff for Bonferroni correction is p = 0.05/33 predictors = p <0.002)

evidence for some associations were stronger among men. Third, evidence for associations with outcomes in other domains (health behavior, social wellbeing, and character and virtue) were modest, mixed, or inconclusive. Fourth, only a few pre-baseline characteristics such as gender and psychological distress predicted subsequent *Ikigai*.

Outcome	E-value for point estimate[b]	E-value for confidence limit[c]
Physical health		
All-cause mortality[d]	1.77	1.00
Functional Disability (Any levels)[d]	2.26	1.74
Functional Disability (Level 1 or greater)[d]	2.30	1.67
Functional Disability (Level 2 or greater)[d]	2.08	1.16
Functional Disability (Need support)[d]	2.17	1.25
Dementia[d]	2.50	1.60
No remaining natural teeth	1.39	1.00
Good self-rated health	1.27	1.00
Instrumental Activity of Daily Living	1.66	1.42
Health behaviors		
Current smoker	1.43	1.00
Body mass index	1.10	1.00
Sedentary lifestyle	2.61	1.39
Flu shot in the past year	1.07	1.00
Infection in the past year (flu)	2.19	1.00
Infection in the past year (pneumonia)	2.57	1.00
Participating health check-up in the past year	1.22	1.00
Insomnia[e]	3.07	1.51
Psychological distress		
Depressive symptoms	2.75	2.45
Hopelessness	4.07	3.35
Social wellbeing		
Frequency of participation in hobby clubs	1.66	1.40
Frequency of participation in sport clubs	1.38	1.05
Frequency of participation in senior clubs	1.18	1.00
Frequency of meeting friends	1.32	1.00
Number of friends I met last month	1.37	1.03
Emotional social support	1.21	1.06
Care social support	1.06	1.00
Subjective wellbeing		
Happiness	2.31	2.05
Pro-social/altruistic behaviors		
Frequency of volunteering	1.32	1.00
Frequency of sharing skills and experiences	1.60	1.36

***Table 4*: Robustness to Unmeasured Confounding (E-values) of Associations Between *Ikigai* and Subsequent Health and Well-being, Japan Gerontological Evaluation Study (n = 6,441)[a].**

[a] For information on calculation on E-values, see VanderWeele and Ding (2017) for the formula.

[b] E-values for effect estimates are the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome, above and beyond the measured covariates, to fully explain away the observed associations of *Ikigai* with the outcomes.

[c] E-values for the 95% confident interval limit closest to the null denote the minimum strength of association on the risk ratio scale that an unmeasured confounder would need to have with both the exposure and the outcome, above and beyond the measured covariates, to shift the 95% confident interval to include the null value.

[d] The analytic sample size was n = 8,951 for the following outcomes: all-cause mortality, functional disabilities, and dementia.

[e] Insomnia was measured one of the submodules in 2016, resulting in substantially smaller sample size (n = 821).

Consistent with prior findings from studies of purpose in life (a conceptual cousin of *Ikigai*), our study showed that *Ikigai* is associated with a lower risk of developing functional disability and dementia.[42,43] Although the precise mechanisms by which *Ikigai* might influence health outcomes have not yet been elucidated, there are at least three potential explanations, some of which can be discussed in the context of our findings regarding outcomes in other domains. First, evidence from purpose in life studies suggests that people with a higher levels of purpose tend to perceive stressors as less stressful and emotionally recover from negative events more quickly, i.e., they are more resilient in adversity.[44,45] *Ikigai* may likewise affect health by buffering the adverse impacts of stressors: this explanation is supported by the observed associations between *Ikigai* and reduced psychological distress and improved subjective wellbeing. Second, *Ikigai* may

motivate some individuals to invest in health-promoting behaviors: for instance, prior results showed an association between higher levels of purpose in life and greater engagement in physical activity. We only found modest evidence that *Ikigai* was associated with lower risk of a sedentary lifestyle and insomnia, which is consistent with prior studies.[46] Future studies assessing health behavior outcomes more comprehensively are warranted. Lastly, *Ikigai* may enhance regulation of physiological systems associated with reduced risk of dementia and physical functioning problems (e.g., reduced inflammatory markers) although evidence has been mixed, and more research is needed.[47]

In contrast to prior purpose studies,[48,49] we did not find substantial evidence that *Ikigai* was associated with all-cause mortality in the whole sample. However, the confidence interval for the estimate was wide (0.60, 1.19) and the point estimate (0.85) was in fact relatively close to that obtained by meta-analyses of the purpose mortality relationship.[48] There was some evidence of the association with lower mortality among men and individuals from higher socioeconomic backgrounds in our sample. The differences may also be explained by conceptual distinctions between purpose in life and *Ikigai*. For example, prior research examining associations between both purpose in life and *Ikigai* with HbA1c—a risk factor of all-cause mortality—observed that purpose in life was strongly associated with lower HbA1c, while *Ikigai* was not.[18] Another possible explanation for the discrepancy is the difference in the operationalization of the exposure variables (continuous or tertiles/quartiles purpose scores in previous research vs. our binary *Ikigai* score).[50] The weak evidence for all-cause mortality in the whole sample was also inconsistent with findings from other *Ikigai* studies,[13–15,51] which observed associations between *Ikigai* and lower all-cause and cardiovascular mortality in Japan. The conflicting results may be attributable to differences in (a) age of the analytic samples (40–79 vs. ≥ 65 in our study), (b) length of follow-up (7 years vs. 3 years in our study), and (c) confounding adjustment—we additionally adjusted for pre-baseline psychological and social wellbeing as potential confounders [9,11,13,14,16] and for prior levels of the outcomes. However, differences in results should not be exaggerated as the confidence interval in the present study for the mortality association was quite wide.

While we observed consistent trends across outcomes for the domains of psychological distress and subjective wellbeing, results were more mixed in other domains. For example, in the social wellbeing domain, *Ikigai* was associated with more frequent participation in hobby clubs, but we observed weak or little evidence of associations with other outcomes in the same domain. Further, in the pro-social/altruistic behaviors domain, *Ikigai* was associated with more frequent sharing of skills and experiences, but we observed little evidence of an association with the frequency of volunteering. This specificity in the *Ikigai*-wellbeing associations within a domain indicates that *Ikigai* might enhance only certain aspects of wellbeing in these domains and not others; understanding why this is so and the mechanisms of action would be an interesting direction for future research. Alternatively, the heterogeneity within domains might be attributable to the differential availability of opportunities to engage in specific social activities. For instance, hobby clubs might be more accessible than other forms of social participation (e.g., sports clubs) in local communities and, hence, more sensitive to the salubrious effect of *Ikigai*, which resulted in the somewhat stronger association between *Ikigai* and hobby club participation.

The sub-group analyses provided two insights. First, *Ikigai* may improve physical health and other domains of wellbeing (e.g., psychological distress) among men but not as substantially among women. A prior study also found the association between *Ikigai* and lower all-cause mortality was stronger among men.[14] Although the reasons for this gender difference remain unclear, it is possibly explained by patriarchal values embedded in Japanese society. Studies from Japan have documented that social participation was associated with improved health more strongly in men than in women, possibly because Japanese men tend to feel more rewarded by having social roles and *Ikigai*.[36,37] Moreover, although speculative, sources of *Ikigai* may differ by gender and contribute to the effect heterogeneity. Future studies need to incorporate information on kind of activities from which people drive *Ikigai*. Second, *Ikigai* may improve some physical health outcomes (e.g., all-cause mortality) among those with high SES but less so for those with low SES, which is consistent with prior evidence that individuals from lower socioeconomic backgrounds may benefit less, health-wise, from having a purpose in life.[38] A potential reason is the socioeconomic heterogeneity in sources to attain *Ikigai*. For example, among individuals who identify "daily exercise" as a source of *Ikigai*, the high SES individuals are able to spend longer time engaging in exercise compared to those with low SES and must rely on other *Ikigai* sources. High SES and low SES individuals may also derive *Ikigai* from different activities that yield collateral health benefits, which is another reason why we need more detailed assessment of the kinds of activities associated with *Ikigai*.

When evaluating potential antecedents of *Ikigai*, we found some evidence of bidirectionality in the association between *Ikigai* and subsequent health and wellbeing. For example, *Ikigai* was associated with decreased depressive symptoms; at the same time, lower depressive symptoms before the baseline were associated with an increased likelihood of having *Ikigai* later. The same trend was observed for hopelessness. However, none of the other pre-baseline levels of the outcomes were strongly predictive of subsequent *Ikigai*. Prior studies of

younger populations identified some predictors (e.g., other aspects of subjective wellbeing) of subsequent changes in purpose in life.[6,52,53] Early randomized controlled trials, ranging from group cognitive behavioral therapy to volunteering, have explored whether a sense of purpose can potentially be altered, but further work is needed on developing *Ikigai* interventions.[3,54–57]

The strengths of our study include: (1) the first use of an outcome-wide design to holistically evaluate associations between *Ikigai* with subsequent health and wellbeing, (2) the use of a large, nationwide, and longitudinal cohort study which helped ensure temporal ordering between the covariates, *Ikigai*, and the outcomes, and (3) a rich adjustment of potential confounders including prior outcome values to address reverse causation. Nonetheless, our study has at least nine limitations. First, our *Ikigai* measure was a single binary item that asked if respondents had *Ikigai* or not. Sone *et al* assessed whether participants had *Ikigai* by asking "Do you have *Ikigai* in your life?" with three response options (yes/uncertain/no). In their analytic sample (n = 43,391), 36.4% indicated they were uncertain, suggesting our binary measure is prone to misclassification.[13] Moreover, we could not assess varying levels of *Ikigai* and its sources, which can result in heterogeneity in the impacts of *Ikigai* on health and wellbeing. Future studies assessing varying levels of *Ikigai* are warranted because such studies will inform whether increasing levels of *Ikigai* among those who already have *Ikigai* might provide additional benefit. Second, although *Ikigai* can be time-varying, we did not have information on when the respondents developed *Ikigai* and how long it had persisted, making the interpretation of our findings difficult. Future studies should adjust for pre-baseline levels of *Ikigai*. Prior *Ikigai* levels were not available in our study, but such an adjustment would allow examining the impact of "changes" in *Ikigai* on health and wellbeing and also help further address potential unmeasured confounding and reverse causation.[20] Third, outcome measures we used in this study were limited by data availability. Most outcomes were based on self-report and crude, hence, susceptible to reporting bias. For example, some people may obtain *Ikigai* from engaging in unhealthy activities (e.g., smoking), and the same individuals may underreport these outcomes. Moreover, we could not assess some important outcomes that could be related to *Ikigai* (e.g., diet for the health behavior domain) as we lacked these information.[58] Fourth, the 3-year follow-up period may have been too short for some of the beneficial effects of *Ikigai* to manifest, which could explain the lack of conclusive evidence for an association with all-cause mortality and other null findings in this study. Our ad-hoc analysis indicated that changes from 2013 to 2016 were relatively small for some outcomes; for example, only 6% of the analytic sample (n=506) died during the three-year follow-up, and only 3% (n=162) experienced changes in the binary self-reported health outcome (Table S9). Fifth, the size of our analytic samples was relatively smaller compared to the previous studies on *Ikigai*.[13,14] The difference in sample size and corresponding power may account for the inconclusive evidence in our study concerning all-cause mortality, since our point estimate was similar to many prior studies, but our confidence interval was wider and included the null. Sixth, selection bias due to selective attrition is possible. The largest sample attrition in this study occurred because the questionnaire containing the *Ikigai* item was distributed to a randomly selected 20% of the original sample (n=54,283 to n=10,867); hence, the attrition is random, and resulting selection bias is likely minimal. However, attrition in other steps of the sample selection might have caused selection bias, and we evaluated this possibility by comparing the distribution of covariates to respondents of the pre-baseline wave survey and the analytic sample; we observed similar distributions between the two samples, which suggests reduced likelihood of selective sample selection (Table S8). Seventh, we cannot entirely preclude the possibility of unmeasured confounding or reverse causation. We adjusted for a comprehensive set of pre-baseline covariates, including prior outcome levels (which tend to be the strongest confounders and cause reverse causation). However, even conditional on the pre-baseline outcome values in 2010, outcome values may change before the exposure assessment in 2013 and independently confound the *Ikigai*-outcome associations. Moreover, we conducted sensitivity analysis for unmeasured confounding and demonstrated some observed associations might be somewhat robust to unmeasured confounding. Eighth, the outcome-wide approach sacrifices depth for breadth, and this is indeed noted in the methodology paper that presents the approach.[21] However, the traditional design focusing on a single or a narrow set of outcomes has other limitations (e.g., not providing holistic evidence on *Ikigai*-health associations, p-hacking, and publication bias), which the outcome-wide design seeks to address, at least to some extent. We think this is a trade-off, and the outcome-wide design (which contains more breadth) and traditional study design (which contains more in-depth discussion) are both complementary and play different roles in the advancement of science. Lastly, these findings are based on a specific population, and the results may not generalize to other populations in which the potential effect modifiers of the associations between *Ikigai* and health/wellbeing (e.g., reasons for having *Ikigai*) are distributed differently across populations.[59]

In conclusion, we found that having *Ikigai* may lead to decreased psychological distress and improved subjective wellbeing among Japanese older adults, as well as improved physical health among Japanese older men and those with high SES. More research is needed to understand the heterogeneous associations with the

outcomes within domains of social wellbeing and prosocial/altruistic behavior as well as the reasons why *Ikigai* appeared less beneficial for some outcomes among women and those with low SES.

Declaration of interests

Authors declare that they have no competing interests.

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Contributors

S.S.O, K.S, I.K, T.J.V. contributed to the conceptualization. S.S.O, K.S contributed to the data curation, formal analysis, methodology, project administration, visualization, validation, and writing original draft. T.J.V., E.S.K., I.K contributed to supervision. S.S.O, K.S, E.S.K, K.S, N.K, T.F, K.K, T.L, C.TF, I.K, T.J.V. contributed to the writing review and editing. K.K, K.S, T.J.V contributed to funding acquisition. K.K, N.K, K.S contributed to investigation (data collection).

Data sharing statement

The dataset supporting the conclusions of this article is available in response to the request from the researchers admitted by the JAGES committee (dataadmin.ml@jages.net). All JAGES datasets have ethical or legal restrictions for public deposition due to inclusion of sensitive information from the human participants. All analyses were conducted in R, version 3.6.0. Code used to generate the results presented in the manuscript are available from the corresponding author upon request.

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Supplementary materials

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