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 < 0.01).

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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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
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), 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.14,15

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

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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”, “wellbeing”, 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.
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. 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 a sense of 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, 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]), 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 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 wellbeing (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. 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. 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). 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. 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
**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 Insurance Database).

LTCI: Long-term care insurance.
the pre-baseline covariates and Ikigai in 2013, simultaneously controlling for all other covariates. Second, to evaluate the robustness of our effect estimates to unmeasured confounding, we calculated E-values for each Ikigai-outcome association. 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. 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. We formally tested for effect measure modification by comparing the subgroup-specific estimates, on both additive (difference in standardized differences for continuous outcomes 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. 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 < 0.05 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...
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).

| Pre-baseline characteristics               | Overall | Ikigai in 2013<sup>a</sup> | p-value<sup>b</sup> |
|--------------------------------------------|---------|----------------------------|--------------------|
|                                            | n = 6,411 | n = 776 | n = 5,205 |
| Sociodemographic factors                   |          |        |          |
| Age, mean (SD)                             | 71.9 (5.1) | 71.8 (4.9) | 71.8 (5.0) | 0.923 |
| Gender, n (%)                              |          |        |          |
| Men                                        | 2,931 (46%) | 309 (40%) | 2,622 (47%) | <0.001 |
| Women                                      | 3,510 (54%) | 467 (60%) | 2,745 (53%) |          |
| Marital status, n (%)                      |          |        |          |
| Married                                    | 4,771 (76%) | 535 (71%) | 3,904 (77%) | <0.001 |
| Widowed                                    | 1,168 (19%) | 145 (19%) | 963 (18%) |          |
| Divorced                                   | 187 (3.0%) | 32 (4.3%) | 153 (2.8%) |          |
| Single                                     | 115 (1.8%) | 27 (3.6%) | 77 (1.6%) |          |
| Other                                      | 35 (0.6%) | 12 (1.6%) | 23 (0.5%) |          |
| Living alone, n (%)                        | 703 (11%) | 115 (15%) | 588 (10%) | <0.001 |
| Education, n (%)                           |          |        |          |
| <6 years                                   | 87 (1.4%) | 16 (2.1%) | 71 (1.3%) | <0.001 |
| 6-9 years                                  | 2,691 (43%) | 409 (54%) | 2,251 (41%) |          |
| 10-12 years                                | 2,271 (36%) | 230 (31%) | 1,938 (37%) |          |
| ≥13 years                                  | 1,204 (19%) | 93 (12%) | 1,102 (20%) |          |
| Other                                      | 28 (0.4%) | 4 (0.5%) | 23 (0.4%) |          |
| Job, n (%)                                 |          |        |          |
| Working                                    | 1,553 (27%) | 154 (23%) | 1,398 (26%) | 0.006 |
| Retired                                    | 3,521 (62%) | 438 (64%) | 3,058 (60%) |          |
| Never worked                               | 644 (11%) | 88 (13%) | 546 (10%) |          |
| Equlized household income (10,000 yen), mean (SD) | 151 (93) | 128 (86) | 150 (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%) | 486 (9.3%) | <0.001 |
| Good self-rated health, n (%)              | 5,489 (87%) | 558 (74%) | 4,943 (88%) | <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%) | 486 (9.4%) | <0.001 |
| Body mass index, mean (SD)                 | 23.1 (5.09) | 22.9 (3.20) | 22.4 (3.16) | 0.3 |
| Participating health check-up in the past year, n (%) | 4,191 (67%) | 440 (59%) | 3,721 (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 (89%) | <0.001 |
| Care social support, n (%)                 | 5,964 (96%) | 659 (89%) | 4,587 (97%) | <0.001 |
| Subjective wellbeing                       |          |        |          |
| Life satisfaction, n (%)                   | 5,235 (83%) | 422 (56%) | 4,773 (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 |

<sup>a</sup> 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.

<sup>b</sup> P-values were calculated using Pearson’s Chi-square test for categorical variables and Wilcoxon rank sum test for continuous variables.
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...
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.

| Predictors in 2010 | RR† | 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) | | | | |
| Number of major life events in the past year | 1.00 | 0.99 | 1.01 | 0.424 | N.S. |
| **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.
† 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.
* 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)
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

| 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 level)    | 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).\(^f\)

\(^a\) 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).
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,45-49 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.49 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.50 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,11-15,51 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 confounders5,11,13,14,16 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.16-37 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 derive 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.18 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. 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. The strengths of our study include: (i) 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. 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.

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. 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. 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.

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, N.K, K.S 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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