PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Purpose in life (Ikigai) and employment status in relation to cardiovascular mortality: the Japan Collaborative Cohort Study
AUTHORS	Miyazaki, Junji; Shirai, Kokoro; Kimura, Takashi; Ikehara, Satoyo; Tamakoshi, Akiko; Iso, Hiroyasu

VERSION 1 – REVIEW

REVIEWER	Erica Sharpe National University of Natural Medicine
REVIEW RETURNED	04-Feb-2022

GENERAL COMMENTS	I found this to be a very strong paper, and it is notable that it followed participants for nearly 30 years. Some questions and suggestions: - Can you indicate where the participants were recruited? - Do you think decreased CVD could be due to some of the other health factors associated with Ikigai? Such as exercise? - What did the unemployed individuals find purpose in? I ask because caregivers (mothers for example) are not employed but have a job/responsibility. If this data is available, it would be interesting to mention. Otherwise, if they had a passion they were working toward turning into a career, that motivation may be similar to employment. I'm curious if you can elaborate on what the unemployed felt their purpose to be. Thank you for this important work.

REVIEWER	Lijing Zhang Beijing University of Chinese Medicine
REVIEW RETURNED	07-Feb-2022

GENERAL COMMENTS	1. The author might improve the reference format. 2. I would suggest the author discuss the potential mechanism of the the potential preventive effect of Ikigai on mortality more detailly. 3. The author might want to do check the accuracy of the datas, such as the total number of CVD deaths in the discussion does not match the items included.

REVIEWER	Masoud Salehi Department of Biostatistics, School of Public Health, Iran University of Medical Sciences
REVIEW RETURNED	14-Mar-2022

GENERAL COMMENTS	The paper is generally well written and structured. However, in my opinion the paper has some shortcomings in regards to some report of the results and methods. It would be helpful to better understand of the followed line by the respectful authors

	In the introduction section, Page 12, Lines 10 and 15 and similar situations, report mean with standard deviation In the methods section, Page 14, Lines 8, there is need more explanation about the trend analysis. It I not clear for me that did you consider the time of event or different determined variable measuring steps in the cohort study and consider it as longitudinal model. It should be cleared in the methods section how you consider different periods of the cohort study in your model. In the results section, Page 15, Lines 45, trend p value need more explanation. In the results section, there is need more explanation of the estimated HR as the Odds Ratio. In table 1, Page 27, Lines 7 and 8, specify the reported statistic.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Erica Sharpe, National University of Natural Medicine
Comments to the Author:
I found this to be a very strong paper, and it is notable that it followed participants for nearly 30 years.
Some questions and suggestions:
- Can you indicate where the participants were recruited?

Response:
We indicate where the participants were recruited as follows:
The Japan Collaborative Cohort Study for the Evaluation of Cancer Risks (JACC study) enrolled residents in 45 area around Japan between1988 and 1990. (page 6, lines 93-94)

- Do you think decreased CVD could be due to some of the other health factors associated with Ikigai? Such as exercise?

Response:
We examined the association between Ikigai and risk of CVD mortality after adjustment for lifestyle habits, including physical activity and walking habits, socioeconomic factors, and other CVD risk factors. The first sentence of the discussion section has revised as follows:
In a large prospective cohort study, higher levels of Ikigai were associated with a lower risk of mortality from total CVD among unemployed men and women after adjustment for known cardiovascular risk factors, but such as inverse association was not observed for the employed. (page 10, lines 196-201)

- What did the unemployed individuals find purpose in? I ask because caregivers (mothers for example) are not employed but have a job/responsibility. If this data is available, it would be interesting to mention. Otherwise, if they had a passion they were working toward turning into a career, that motivation may be similar to employment. I'm curious if you can elaborate on what the unemployed felt their purpose to be.

Response:
Thank you for your interesting comment. However, we did not have the information whether caregivers have a job / responsibility and what the unemployed felt their purpose of being.

Homemakers were regarded as the category of employed because they were primarily women, and many of them were assumed to have motivation for children and housework in Japan. (page 8, lines 148-150; page 11, lines 223-229)

Thank you for this important work.
Response:
We appreciate your careful peer review and comments.

Reviewer: 2
Dr. Lijing Zhang, Beijing University of Chinese Medicine
Comments to the Author:
1. The author might improve the reference format.

Response:
We have improved the format of the references. (page 15-19, lines 310-396)

2. I would suggest the author discuss the potential mechanism of the the potential preventive effect of Ikigai on mortality more detailly.

Response:
A previous study reported that people with a purpose in life have lower levels of the soluble IL-6 receptor, an inflammatory marker associated with stroke and cardiovascular disease, which has been added to the discussion section to strengthen the explanation of the biological mechanisms for purpose in life. (page 11, lines 209-211)

3. The author might want to do check the accuracy of the datas, such as the total number of CVD deaths in the discussion does not match the items included.

Response:
The number of total CVD deaths did not match the summing number of CVD types because 'other CVDs' were not presented. The same was true for stroke of undetermined type. Therefore, 'other CVDs' and 'stroke of undetermined type' were included in the abstract, methods, results, and Table 4.

Reviewer: 3
Prof. Masoud Salehi, Department of Biostatistics, School of Public Health, Iran University of Medical Sciences
Comments to the Author:
The paper is generally well written and structured. However, in my opinion the paper has some shortcomings in regards to some report of the results and methods. It would be helpful to better understand of the followed line by the respectful authors

In the introduction section, Page 12, Lines 10 and 15 and similar situations, report mean with standard deviation

Response:
We revised your notation from mean to age range. (page 5, lines 74, 81)

In the methods section, Page 14, Lines 8, there is need more explanation about the trend analysis.

Response:

We added more explanation about the trend analysis as follows:
To test for linear trends across the Ikigai categories for baseline risk characteristics and hazard ratios, and ordering variable of Ikigai (1: low, 2: moderate, 3: high) was used. (page 8, lines 153-154)

It I not clear for me that did you consider the time of event or different determined variable measuring steps in the cohort study and consider it as longitudinal model. It should be cleared in the methods section how you consider different periods of the cohort study in your model.

Response:
We revised the description of the analysis as follows:
The analysis used a Cox proportional hazards model to calculate sex-specific hazard ratios (HRs) and 95% confidence intervals (CIs) of CVD according to perceived levels of Ikigai at baseline and the risk of mortality from CVD at follow-up. (page 8, lines 136-138)

In the results section, Page 15, Lines 45, trend p value need more explanation.

Response:
Again, we added the following sentence:
To test for linear trends across the Ikigai categories for baseline risk characteristics and hazard ratios, and ordering variable of Ikigai (1: low, 2: moderate, 3: high) was used. (page 8, lines 153-154)

In the results section, there is need more explanation of the estimated HR as the Odds Ratio.

Response:
We described that HRs, not odds ratios, were calculated using the Cox proportional hazards model.

In table 1, Page 27, Lines 7 and 8, specify the reported statistic.

Response:
We added to report the statistics to Table 1. (page 20, 21)