

## RESEARCH QUESTION

Are carbohydrate and fat intakes associated with risk of mortality among the Japanese population?



## METHODS

Nationwide follow-up survey in Japan



J-MICC Study 81,333 people

Exposure

Outcome



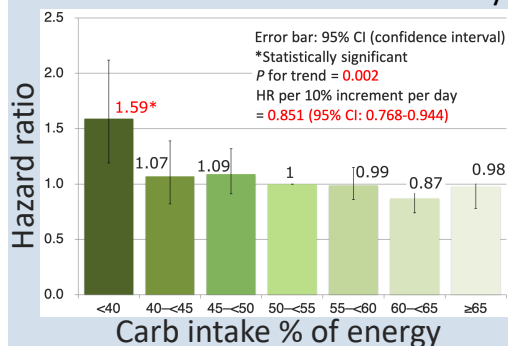
Carbohydrate and fat intakes



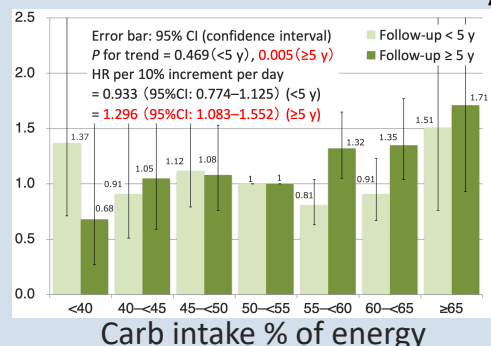
Death

**RESULTS** Number of death: 1,838 in 34,893 men, 945 in 46,440 women (Mean follow-up period: 8.9 years)

### Carb intake in men and mortality



### Carb intake in women and mortality



## CONCLUSIONS

Low-carb diet in men and high-carb diet in women are significantly associated with a higher risk of mortality.

### Association between carbohydrate and fat intakes and risk of mortality

– Extreme dietary habits can affect life expectancy –

#### SUMMARY

Dr. Takashi Tamura and Prof. Kenji Wakai from Department of Preventive Medicine, Nagoya University Graduate School of Medicine, and their collaborators conducted a cohort study<sup>\*1</sup> to investigate the association between carbohydrate and fat intakes and the risk of mortality among the Japanese population, using follow-up survey data from the Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study [principal investigator: Dr. Keitaro Matsuo from Division of Cancer Epidemiology and Prevention, Aichi Cancer Center Research Institute])<sup>\*2</sup>. They discovered that a low carbohydrate intake in men and a high carbohydrate intake in women were associated with higher risks of all-cause and cancer mortality. They also found that fat intake in women had potential to lower the risk of all-cause mortality. This study was supported by a JSPS KAKENHI Grant 'CoBiA' from the Japanese Ministry of Education, Culture, Sports, Science and Technology.

Restricting intakes of carbohydrates and fats (i.e., advocating low-carbohydrate and low-fat diets) is considered beneficial for the prevention of lifestyle diseases as it promotes weight loss and improves blood glucose levels. However, the long-term associations, specifically whether these dietary habits contribute to longer life expectancy, remain unclear. Recent epidemiological studies<sup>\*3</sup> in various countries, including Western countries, suggest that extreme dietary habits for carbohydrates and fats are associated with a higher risk of mortality. Due to the discrepancy between the short-term benefits and the long-term life expectancy associated with low-carbohydrate and low-fat diets, there is increasing international interest on this issue. To date, there is limited evidence specifically from East Asian populations, including Japanese individuals who consume more carbohydrates and less fats than individuals in Western countries.

This research group, therefore, conducted a follow-up survey over a period of 9 years with approximately 81,000 participants from the J-MICC study to evaluate the association between carbohydrate and fats intakes and the risk of mortality among the Japanese population. The participants' daily dietary intakes of carbohydrates, fats, and energy

were estimated using a food frequency questionnaire<sup>\*4</sup>, and calculated as a percentage of total energy intake<sup>\*5</sup> for carbohydrates and fats (1 gram of carbohydrates and fats provides 4 kcal and 9 kcal of energy, respectively). For men, the group with a low carbohydrate intake (<40%) had a 1.59-fold higher risk of all-cause mortality and a 1.48-fold higher risk of cancer mortality (*P* for trend<sup>\*6</sup> = 0.002 and 0.071, respectively), compared with the reference group of carbohydrate intake of 50–<55%. Among women with a follow-up period of 5 years or longer, those with a high carbohydrate intake (≥65%) had a 1.71-fold higher risk of all-cause mortality (*P* for trend = 0.005), compared with the reference group of carbohydrate intake of 50–<55%. A similar association was observed for the risk of cancer mortality (*P* for trend = 0.003). Regarding the association between fat intake and risk of mortality, men with a high fat intake (≥35%) had a 1.79-fold higher risk of cancer mortality, compared with the reference group of fat intake of 20–<25%. The risk of cardiovascular disease (CVD) mortality increased with fat intake in men (*P* for trend = 0.020). On the other hand, fat intake in women showed a marginal inverse association with the risk of all-cause and cancer mortality (*P* for trend = 0.054 and 0.058, respectively).

The findings from this research group suggest a reconsideration of dietary habits that promote a low-carbohydrate or high-carbohydrate diet, and emphasize the importance of moderating fat intake. This study was published online by *The Journal of Nutrition* on June 2, 2023.

#### **KEY POINTS:**

- Extreme dietary habits for carbohydrates and fats have an impact on long-term life expectancy.
- Recommending a low-carbohydrate diet and restricting a high-fat diet may not necessarily be beneficial.
- The importance of a dietary balance is suggested for future mortality risk.

## **1. BACKGROUND**

Low-carbohydrate and low-fat diets are considered for promoting weight loss and improving blood glucose levels, making them potentially beneficial for the prevention of lifestyle diseases. However, the long-term associations, specifically whether these dietary habits contribute to longer life expectancy, remain unclear. Recent epidemiological studies in various countries, including Western countries, suggest that extreme dietary habits for carbohydrates and fats are associated with a higher risk of mortality. Due to the discrepancy between the short-term benefits and the long-term life expectancy associated with low-carbohydrate and low-fat diets, there is increasing international interest on this issue. To date, there is limited evidence specifically from East Asian populations, including Japanese individuals who consume more carbohydrates and less fats than individuals in Western countries. This research group, therefore, aimed to evaluate the association between carbohydrate and fat intakes and risk of mortality among the Japanese population, using follow-up survey data from the Japan Multi-Institutional Collaborative Cohort Study (J-MICC study).

## **2. METHODS**

The subjects consisted of 34,893 men and 46,440 women who had participated in the baseline survey of the J-MICC study, with all the necessary data available and without medical history of cancer or cardiovascular diseases (CVD). The mean follow-up period is approximately 9 years. The daily dietary intakes of carbohydrates,

fats, and energy were estimated using a food frequency questionnaire, and calculated as a percentage of total energy intake for carbohydrates and fats (1 gram of carbohydrates and fats provides 4 kcal and 9 kcal of energy, respectively). We adjusted for confounding factors<sup>\*7</sup> such as smoking and alcohol consumption that have a significant impact on risk of mortality in the analysis.

### 3. RESULTS

Figure 1 shows the association between carbohydrate intake and risk of mortality in men. The group with a low carbohydrate intake (<40%) showed a 1.59-fold higher risk of all-cause mortality ( $P$  for trend = 0.002) and a 1.48-fold higher risk of cancer mortality ( $P$  for trend = 0.071) compared with the reference group of carbohydrate intake of 50–<55%. The group with a moderately low carbohydrate intake (45–<50%) had a 2.32-fold higher risk of CVD mortality ( $P$  for trend = 0.002). In the analysis for refined carbohydrate intake (i.e., rice, bread, noodles, Western sweets, and Japanese confectionery) and minimally processed carbohydrate intake, similar associations were observed; low intakes of both refined and minimally processed carbohydrate were significantly associated with the risk of all-cause mortality (see Supplementary Tables 1–2 in the original article).

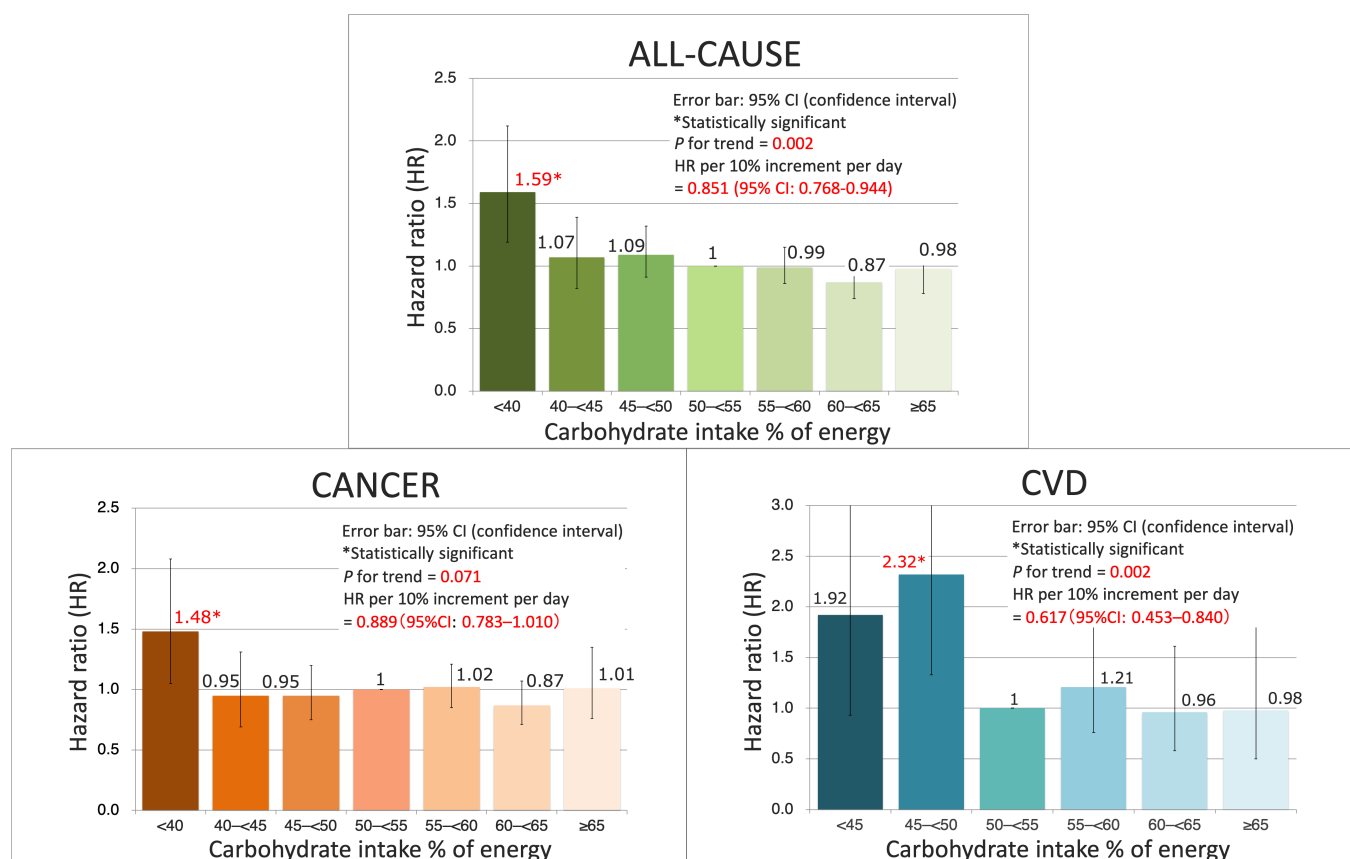


Fig.1 Associations between carbohydrate intake and risk of mortality in men.

Figure 2 shows the association between carbohydrate intake and the risk of mortality in women. Because the proportional hazards assumption<sup>\*8</sup> for the association in women was slightly violated (i.e., the impact of carbohydrate intake on risk of mortality depended on the follow-up duration), the analysis was performed by dividing the follow-up period into 5-year intervals (i.e., approximately half of the median follow-up period).

Among women with the follow-up period of 5 years or longer, those with a high carbohydrate intake ( $\geq 65\%$ ) had a 1.71-fold higher risk of all-cause mortality ( $P$  for trend = 0.005), compared with the reference group of carbohydrate intake of 50–<55%. A similar association was observed for the risk of cancer mortality ( $P$  for trend = 0.003). When the follow-up period is less than 5 years, the groups with a moderately low carbohydrate intake (45–<50%) and a moderately high carbohydrate intake ( $\geq 60\%$ ) were associated with a 4.04-fold and a 3.46-fold higher risk of CVD mortality, respectively. In the analysis for refined carbohydrate and minimally processed carbohydrate intakes, no clear associations were observed (see Supplementary Tables 3–4 in the original article).

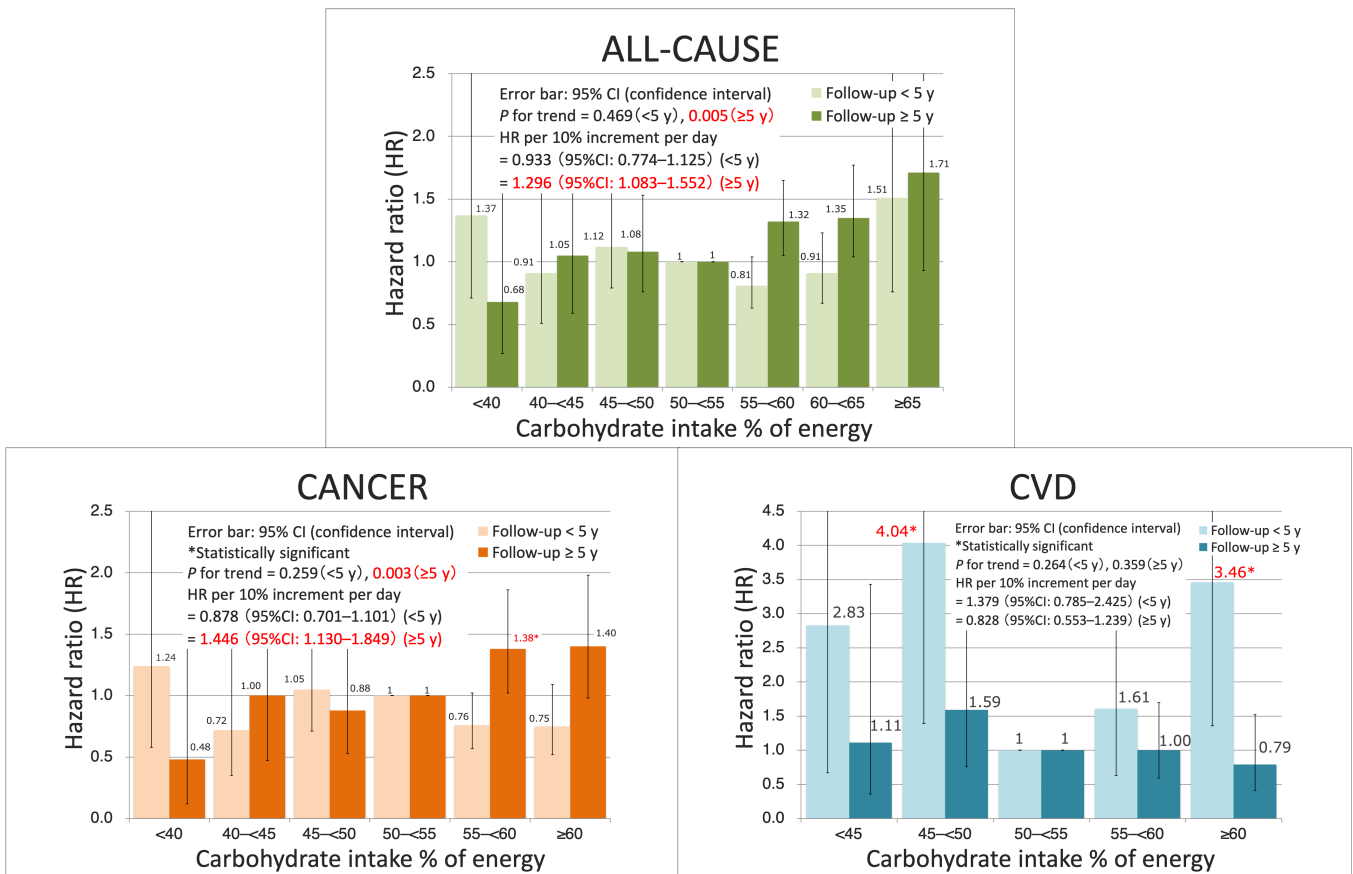


Fig.2 Associations between carbohydrate intake and risk of mortality in women.

Figure 3 shows the association between fat intake and risk of mortality in men. The group with a high fat intake ( $\geq 35\%$ ) had a 1.79-fold higher risk of cancer mortality, compared with the reference group of fat intake of 20–<25%. Fat intake in men was positively associated with the risk of CVD mortality ( $P$  for trend = 0.020). In the analysis for saturated fat intake (abundant in meat, dairy products, and processed foods) and unsaturated fat intake (abundant in fish, vegetable oils, and nuts), those with a lower intake of unsaturated fat had a higher risk of all-cause and cancer mortality (see Supplementary Tables 5–6 in the original article).

Figure 4 shows the association between fat intake and risk of mortality in women. Fat intake in women showed a marginal inverse association with the risks of all-cause and cancer mortality ( $P$  for trend = 0.054 and 0.058, respectively). Similar associations were observed for saturated fat intake, but no clear correlations were

found for unsaturated fat intake in women (see Supplementary Tables 7–8 in the original article).

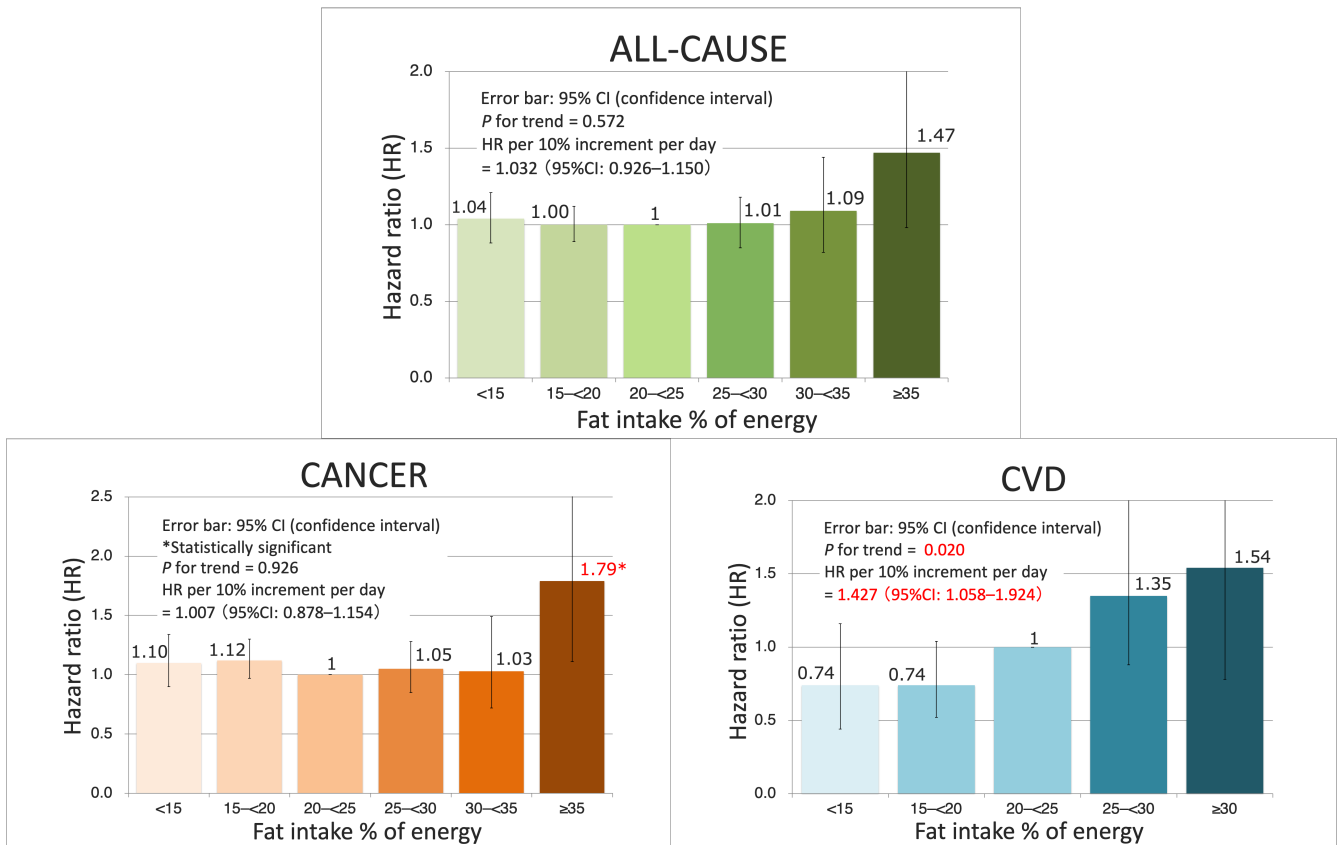


Fig.3 Associations between fat intake and risk of mortality in men.

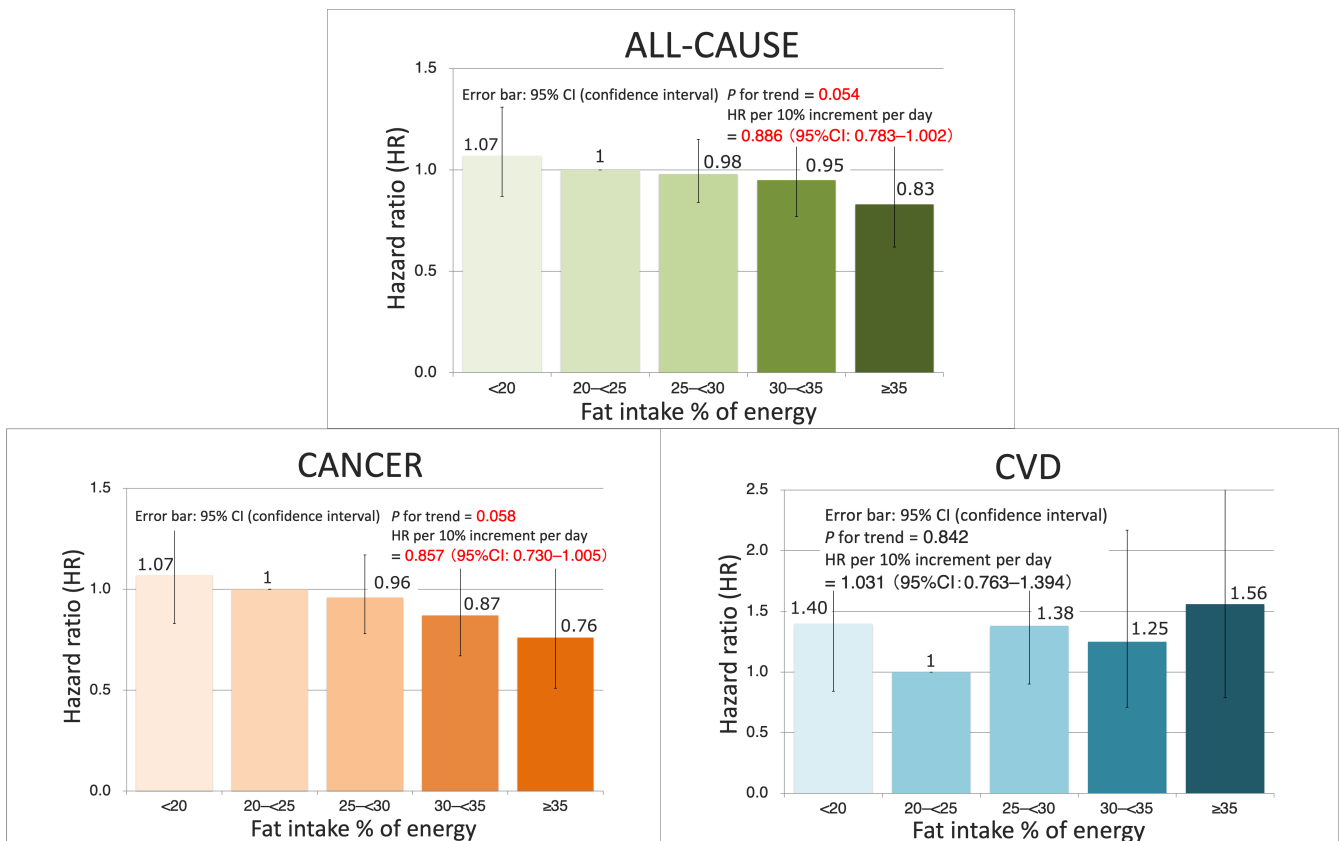


Fig.4 Associations between fat intake and risk of mortality in women.

#### 4. FUTURE DIRECTIONS

This study showed the potential impact of extreme carbohydrate and fat intakes on the risk of mortality among the Japanese population, after controlling for confounding factors such as smoking status and alcohol consumption. It suggests a reconsideration of effects of dietary habits on risk of mortality, indicating low-carbohydrate or high-carbohydrate diets could not be beneficial, and emphasizing the importance of moderating fat intake. A longer follow-up survey of the J-MICC study with a larger number of cases will enable more detailed analyses of specific causes of death and evaluations based on different cancer sites. The authors anticipate that these findings will be reproduced in the general Japanese population through other studies, as well as the exploration and elucidation of molecular biological mechanisms.

#### 5. GLOSSARY

\*<sup>1</sup> **Cohort study:** a type of study that follows a group of individuals with a particular characteristic and a group without that characteristic over time to assess differences in future outcomes such as mortality rates and disease incidence. Cohort studies allow for the examination of various factors and their associations with outcomes. By recoding the characteristics of individuals before the occurrence of outcomes and tracking the outcomes over a long period, cohort studies can provide reliable evidence.

\*<sup>2</sup> **The Japan Multi-Institutional Collaborative Cohort Study (J-MICC Study):** This study is a nationwide follow-up survey conducted over a 20-year period, involving approximately 100,000 participants in Japan. Its aim is to identify factors that make individuals more susceptible to certain diseases by following the health status of participants, including cancer incidence and mortality. The survey was launched in 2005 and is currently being carried out by 13 research groups in Japan. This study examines not only participants' lifestyle habits but also their genetic background in order to explore the underlining causes of diseases. It is the first large-scale molecular epidemiological cohort study in Japan.

\*<sup>3</sup> **Epidemiological research:** a general term for studies that investigate factors related to diseases and health in human populations. Recently, it has become common to analyze large-scale epidemiological survey data to evaluate differences in mortality rates and disease incidence, taking into account not only lifestyle factors but also genetic factors. This research plays a crucial role in disease prevention and the development of public health policies.

\*<sup>4</sup> **Food frequency questionnaire:** a tool used to assess the frequency and quantity of food intake, listing specific food items such as soybeans, small fish, yogurt, and green tea. Participants select responses from the provided options to indicate how often they consume each food and beverage and the portion size during the past year. Based on the responses to this questionnaire, dietary nutrient and food group intakes can be estimated. The purpose of this questionnaire is to understand an individual's dietary habits or trends in nutrient intakes. By combining estimated nutrient intakes with lifestyle and follow-up data, accurate evaluations of their impact on health can be made.

\*<sup>5</sup> **Percentage of energy intake (%):** it refers to the proportion of energy derived from specific nutrients out

of the total energy intake and serves as an indicator of dietary balance. The percentage of energy intake is used in nutritional surveys, epidemiological studies, and the development of dietary guidelines.

\*<sup>6</sup> **P for trend:** it is a statistical measure used to evaluate the significance and relevance of a dose-response relationship between exposure and outcome. It clarifies whether the association between causes and results is due to chance, and emphasizes that a lower *P*-value (typically below 0.05) suggests a higher likelihood that the association is not simply a result of chance.

\*<sup>7</sup> **Confounding factors:** factors not being studied that meet the following three conditions: 1) they influence the outcome, 2) they are correlated with the factors being studied, and 3) they are not intermediate factors between the factors being studied and the outcome. If confounding factors are not properly controlled, spurious associations (i.e., incorrect associations caused by other factors) may be observed, highlighting the importance of controlling confounding factors to accurately infer causal relationships.

\*<sup>8</sup> **Proportional hazards assumption:** it refers to the property where the hazard ratio (ratio of risks) between compared groups remains constant over time and is not time-dependent. This is one of the conditions that a factor should satisfy when conducting analysis using the proportional hazards regression model.

## 6. JOURNAL OF PUBLICATION

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