

## Dietary Habits and Stomach Cancer Risk in the JACC Study

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**BACKGROUND:** Despite a declining incidence, stomach cancer is still a dominant cancer in Japan. The association between dietary habits and stomach cancer risk was investigated in a large prospective study in Japan.

**METHODS:** Data were obtained using a self-administered questionnaire from 1988 through 1990. Food frequency questionnaire was used to evaluate the consumption of 33 selected food items. Proportional hazard model was used to determine the hazard ratios (HRs) and their 95% confidence intervals (CIs) of stomach cancer for different levels of the dietary intakes.

**RESULTS:** A western style breakfast showed an inverse association with stomach cancer risk in males (HR=0.49, 95% CI: 0.35-0.70). Women who consumed liver three to four times per week and more than once per day had a significant increased risk, respectively (HR=2.02, 95% CI: 1.12-3.63, HR=3.16, 95% CI: 1.16-8.62). A clear dose-response relationship between the intake of liver and stomach cancer risk was observed. We found no association between stomach cancer mortality and the consumption of fruit such as mandarin orange, and vegetables such as carrots and spinach in both men and women. The consumption of high salt foods such as miso soup and pickles was also not significantly associated with the mortality of stomach cancer in both sexes.

**CONCLUSION:** This prospective study suggested that a western-style breakfast is associated with a lower risk of stomach cancer, although some differences in the association were seen between men and women.

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Steady declines in incidence and mortality rates of stomach cancer have been found worldwide in recent decades.<sup>1</sup> Despite a declining incidence, stomach cancer is still a dominant cancer in Japan.<sup>2</sup> Previous studies indicated that environmental factors, particularly diet, play an important role in the etiology of this cancer.<sup>3,4</sup> An increased risk of stomach cancer has been linked to low dietary intake of fresh fruit and vegetables and a high consumption of starch foods.<sup>5-10</sup> Other reports have suggested that the risk of stomach cancer increased in a population who consumed cured or preserved fish and meat in salt or smoked.<sup>11-13</sup> However, most of this epidemiologic evidence was based on studies with a case-control design. The results from case-control studies can be biased by differential recall of dietary intake due to stomach disorders. Recall of dietary intake could also have been influenced by current dietary habits. Prospective studies are less susceptible to recall bias because dietary intake is measured before the presence of a disease is known. Unfortunately, there have been a limited number of prospective studies in Japan.<sup>14-16</sup> In addition, these studies have less information on lifestyle and the number of subjects was small.

Monbusho cohort study, a large-scale prospective cohort study on life style including dietary habits and cancer, began in 1988 with about 125,000 men and women. This cohort study was conducted by more than twenty universities and research institutes that were located throughout Japan. Therefore, data in this cohort would be representative of the Japanese population. We have investigated the relation between dietary intakes and mortality of stomach cancer.

## METHODS

### *JACC study*

The Japan Collaborative Cohort Study (JACC Study) for Evaluation of Cancer Risk sponsored by the Ministry of Education, Science, Sports and Culture of Japan (Monbusho) was established from 1988 through 1990 to investigate the relationship between various lifestyle variables and cancer mortality and incidence. The study methods have been described in detail elsewhere.<sup>17</sup> In brief, this cohort consisted of 110,792 persons aged 40 -79 years who lived 52 cities, towns and villages in Japan at the beginning of the study. At baseline, the cohort members completed a self-administered questionnaire on dietary habits, smoking, alcohol use, medical history, personal and family history of cancer and demographic data. We followed the subjects from 1988 through 1999. Information on deaths among the study subjects was annually collected by examination of death certificates with permission of the Management and Coordination Agency of the Japanese Government. All baseline data and follow up data including death data were reported to the central committee office. The underlying causes of death were coded according to International Classification of Disease Revision 9 from 1988 through 1994 and after 1995, Revision 10. Stomach cancer was determined by the coding 151.0-159.0 for ICD-9 and C16.0-

C16.9 for ICD-10. Informed consent was obtained from each subject.

To participate in the study, an individual's informed consent was obtained in 36 out of 45 areas (written consent in 35 areas and oral consent in 1 area), though in 9 areas, group consent from head of the area was obtained.

### *Dietary questionnaire*

The dietary section of the questionnaire was a 33 item food frequency questionnaire dealing with on the usual consumption of food and beverages. Frequency consumption of 33 foods was classified into five categories (almost never, less than once or twice per month, once or twice per week, three or four times per week, or almost daily). Food items of vegetables and fruits include spinach, carrot/pumpkin, tomato, cabbage, Chinese cabbage, edible wild plants, fried vegetables, mandarin orange, fresh fruit juice, and others fruits. Regarding four beverages (coffee, black tea, green tea, and oolong tea), participants were asked to choose one of five categories (almost never, 1 to 2 cups per month, 1 to 2 cups per week, 3 to 4 cups per week, or almost daily). Additionally, if they take these beverages almost daily, they were also asked to report the number of cups. For miso soup, the frequency of consumption (almost never, several times per month, every other day, or almost daily) was asked, and the number of cups per day was obtained if subjects chose the category of 'almost daily'. Alcohol intake was based on the usual weekly intake of Japanese sake, beer, wine, whiskey and distilled spirits among current drinkers. In the above described foods, data of some food items were not collected in a few study areas because a different questionnaire was used there.

### *Data analysis*

Proportional hazard model was used to determine hazard ratios (HRs) and their 95% confidence intervals (CIs) of stomach cancer for different levels of the dietary intakes. Analyses were conducted separately for males and females. Statistical significance (two sided) was based on the ratio of the regression coefficient and its standard error. Statistical analysis (PHREG procedure) was performed by the Statistical Analysis System® (SAS institute, 1983).

## RESULTS

During the follow up period, a total of 859 stomach cancer deaths (574 males and 285 females) were obtained. The results of age adjusted analyses are presented in Table 1. There was a non-significant inverse association between the intake of vegetables such as carrots, tomatoes and spinach, and stomach cancer risk in both sexes. There was a weak non-significant association between the intake of cabbage and Chinese cabbage, and mortality among females. The relative risk of fruit consumption such as mandarin orange and pure fruit juice also did not decrease among men and women. In contrast to these results, the consumption of mushroom was associated with the increased risk of stomach cancer in

**Table 1.** Age adjusted hazard ratios of stomach cancer for intake of vegetables, fruit, and other foods by sex.

|                           | Male         |              |                         |             | Female       |              |                         |             |
|---------------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                           | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Spinach</b>            |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 34           | 1.00         | (reference)             |             | 10           | 1.00         | (reference)             |             |
| 1-2/week                  | 121          | 1.16         | 0.79 - 1.69             |             | 50           | 1.29         | 0.65 - 2.55             |             |
| 3-4/week                  | 119          | 1.10         | 0.75 - 1.62             |             | 67           | 1.51         | 0.78 - 2.93             |             |
| 1+/day                    | 162          | 1.29         | 0.89 - 1.87             | 0.16        | 79           | 1.40         | 0.72 - 2.70             | 0.38        |
| <b>Carrot • pumpkin</b>   |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 71           | 1.00         | (reference)             |             | 24           | 1.00         | (reference)             |             |
| 1-2/week                  | 150          | 1.28         | 0.96 - 1.69             |             | 56           | 0.86         | 0.54 - 1.39             |             |
| 3-4/week                  | 98           | 1.19         | 0.88 - 1.61             |             | 64           | 1.04         | 0.65 - 1.67             |             |
| 1+/day                    | 59           | 1.14         | 0.80 - 1.61             | 0.60        | 54           | 1.15         | 0.71 - 1.86             | 0.24        |
| <b>Tomato</b>             |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 145          | 1.00         | (reference)             |             | 72           | 1.00         | (reference)             |             |
| 1-2/week                  | 127          | 1.05         | 0.83 - 1.33             |             | 52           | 0.80         | 0.56 - 1.15             |             |
| 3-4/week                  | 82           | 1.06         | 0.81 - 1.39             |             | 43           | 0.91         | 0.62 - 1.32             |             |
| 1+/day                    | 62           | 1.19         | 0.88 - 1.61             | 0.29        | 44           | 1.10         | 0.76 - 1.60             | 0.66        |
| <b>Cabbage</b>            |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 53           | 1.00         | (reference)             |             | 15           | 1.00         | (reference)             |             |
| 1-2/week                  | 116          | 0.81         | 0.59 - 1.12             |             | 49           | 1.01         | 0.57 - 1.81             |             |
| 3-4/week                  | 113          | 0.90         | 0.65 - 1.25             |             | 56           | 1.16         | 0.65 - 2.04             |             |
| 1+/day                    | 111          | 1.11         | 0.80 - 1.54             | 0.15        | 71           | 1.49         | 0.85 - 2.60             | 0.03        |
| <b>Chinese cabbage</b>    |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 67           | 1.00         | (reference)             |             | 33           | 1.00         | (reference)             |             |
| 1-2/week                  | 122          | 0.99         | 0.73 - 1.33             |             | 58           | 1.03         | 0.67 - 1.58             |             |
| 3-4/week                  | 86           | 0.94         | 0.68 - 1.30             |             | 41           | 0.94         | 0.60 - 1.49             |             |
| 1+/day                    | 77           | 1.18         | 0.85 - 1.64             | 0.39        | 47           | 1.30         | 0.83 - 2.03             | 0.31        |
| <b>Edible wild plants</b> |              |              |                         |             |              |              |                         |             |
| None                      | 137          | 1.00         | (reference)             |             | 71           | 1.00         | (reference)             |             |
| 1-2/month                 | 151          | 1.16         | 0.92 - 1.46             |             | 75           | 1.26         | 0.91 - 1.74             |             |
| 1-2/week                  | 51           | 1.02         | 0.74 - 1.41             |             | 26           | 1.05         | 0.67 - 1.65             |             |
| 3-4/week or more          | 48           | 1.37         | 0.98 - 1.90             | 0.16        | 22           | 1.22         | 0.75 - 2.96             | 0.87        |
| <b>Mandarin orange</b>    |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 94           | 1.00         | (reference)             |             | 23           | 1.00         | (reference)             |             |
| 1-2/week                  | 87           | 0.77         | 0.57 - 1.03             |             | 33           | 0.90         | 0.53 - 1.53             |             |
| 3-4/week                  | 84           | 0.79         | 0.59 - 1.06             |             | 43           | 1.00         | 0.60 - 1.66             |             |
| 1+/day                    | 124          | 0.92         | 0.71 - 1.21             | 0.80        | 93           | 1.03         | 0.65 - 1.63             | 0.65        |
| <b>Pure fruit juice</b>   |              |              |                         |             |              |              |                         |             |
| None                      | 90           | 1.00         | (reference)             |             | 48           | 1.00         | (reference)             |             |
| 1-2/month                 | 60           | 0.91         | 0.66 - 1.26             |             | 19           | 0.68         | 0.40 - 1.17             |             |
| 1-2/week                  | 69           | 0.77         | 0.56 - 1.06             |             | 38           | 1.03         | 0.67 - 1.58             |             |
| 3-4/week                  | 54           | 0.85         | 0.61 - 1.20             |             | 34           | 1.20         | 0.77 - 1.86             |             |
| 1+/day                    | 67           | 1.23         | 0.89 - 1.68             | 0.51        | 31           | 0.95         | 0.60 - 1.49             | 0.59        |
| <b>Bean curd</b>          |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 31           | 1.00         | (reference)             |             | 11           | 1.00         | (reference)             |             |
| 1-2/week                  | 140          | 1.12         | 0.76 - 1.65             |             | 60           | 1.24         | 0.65 - 2.36             |             |
| 3-4/week                  | 162          | 1.09         | 0.74 - 1.60             |             | 88           | 1.38         | 0.74 - 2.59             |             |
| 1+/day                    | 139          | 1.07         | 0.73 - 1.58             | 0.97        | 85           | 1.41         | 0.75 - 2.64             | 0.25        |
| <b>Mushroom</b>           |              |              |                         |             |              |              |                         |             |
| 1-2/month or less         | 152          | 1.00         | (reference)             |             | 46           | 1.00         | (reference)             |             |
| 1-2/week                  | 123          | 0.88         | 0.69 - 1.11             |             | 67           | 1.15         | 0.79 - 1.67             |             |
| 3-4/week                  | 66           | 0.97         | 0.72 - 1.29             |             | 53           | 1.54         | 1.03 - 2.28             |             |
| 1+/day                    | 26           | 0.89         | 0.59 - 1.35             | 0.57        | 17           | 1.11         | 0.64 - 1.94             | 0.16        |

**Table 2.** Age-adjusted hazard ratios of stomach cancer for intake of salty foods by sex.

|                                   | Male         |              |                         |             | Female       |              |                         |             |
|-----------------------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                                   | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Pickles</b>                    |              |              |                         |             |              |              |                         |             |
| 1-2/month or less                 | 52           | 1.00         | (reference)             |             | 18           | 1.00         | (reference)             |             |
| 1-2/week                          | 60           | 1.04         | 0.72 - 1.51             |             | 30           | 1.56         | 0.87 - 2.81             |             |
| 3-4/week                          | 74           | 1.00         | 0.70 - 1.42             |             | 32           | 1.32         | 0.74 - 2.36             |             |
| 1+/day                            | 330          | 1.09         | 0.82 - 1.47             | 0.48        | 175          | 1.47         | 0.90 - 2.39             | 0.26        |
| <b>Fish boiled in soy sauce</b>   |              |              |                         |             |              |              |                         |             |
| None                              | 96           | 1.00         | (reference)             |             | 46           | 1.00         | (reference)             |             |
| 1-2/month                         | 100          | 0.86         | 0.65 - 1.13             |             | 46           | 0.99         | 0.66 - 1.49             |             |
| 1-2/week                          | 104          | 0.88         | 0.67 - 1.17             |             | 50           | 1.09         | 0.73 - 1.63             |             |
| 3-4/week                          | 66           | 1.08         | 0.79 - 1.48             |             | 25           | 0.99         | 0.61 - 1.61             |             |
| 1+/day                            | 30           | 0.92         | 0.61 - 1.38             | 0.87        | 24           | 1.57         | 0.95 - 2.57             | 0.18        |
| <b>Boiled beans</b>               |              |              |                         |             |              |              |                         |             |
| None                              | 80           | 1.00         | (reference)             |             | 29           | 1.00         | (reference)             |             |
| 1-2/month                         | 141          | 0.86         | 0.65 - 1.13             |             | 70           | 0.84         | 0.54 - 1.29             |             |
| 1-2/week                          | 93           | 0.77         | 0.57 - 1.05             |             | 48           | 0.79         | 0.50 - 1.26             |             |
| 3-4/week                          | 73           | 1.19         | 0.86 - 1.63             |             | 34           | 0.97         | 0.59 - 1.60             |             |
| 1+/day                            | 27           | 0.93         | 0.60 - 1.44             | 0.61        | 16           | 0.84         | 0.46 - 1.56             | 0.88        |
| <b>Dried or salty fish</b>        |              |              |                         |             |              |              |                         |             |
| None                              | 36           | 1.00         | (reference)             |             | 29           | 1.00         | (reference)             |             |
| 1-2/month                         | 83           | 0.89         | 0.60 - 1.32             |             | 39           | 0.64         | 0.40 - 1.04             |             |
| 1-2/week                          | 141          | 0.93         | 0.65 - 1.34             |             | 63           | 0.66         | 0.42 - 1.02             |             |
| 3-4/week                          | 66           | 0.85         | 0.57 - 1.28             |             | 33           | 0.69         | 0.42 - 1.13             |             |
| 1+/day                            | 48           | 1.14         | 0.74 - 1.76             | 0.64        | 24           | 0.92         | 0.53 - 1.58             | 0.86        |
| <b>Miso soup</b>                  |              |              |                         |             |              |              |                         |             |
| None                              | 15           | 1.00         | (reference)             |             | 12           | 1.00         | (reference)             |             |
| Several times/month               | 43           | 1.42         | 0.79 - 2.56             |             | 25           | 1.38         | 0.69 - 2.74             |             |
| Several times/week                | 57           | 1.50         | 0.85 - 2.65             |             | 28           | 1.18         | 0.60 - 2.31             |             |
| Everyday                          | 415          | 1.44         | 0.86 - 2.42             | 0.36        | 201          | 1.46         | 0.81 - 2.61             | 0.19        |
| <b>Miso soup(cup)</b>             |              |              |                         |             |              |              |                         |             |
| less than 1/day                   | 115          | 1.00         | (reference)             |             | 65           | 1.00         | (reference)             |             |
| 1/day                             | 93           | 0.90         | 0.69 - 1.19             |             | 65           | 1.21         | 0.86 - 1.72             |             |
| 2/day                             | 114          | 0.99         | 0.76 - 1.28             |             | 62           | 1.24         | 0.87 - 1.77             |             |
| 3+/day                            | 140          | 1.17         | 0.91 - 1.50             | 0.16        | 41           | 1.24         | 0.84 - 1.84             | 0.23        |
| <b>Preference for salty foods</b> |              |              |                         |             |              |              |                         |             |
| No                                | 9            | 1.00         | (reference)             |             | 4            | 1.00         | (reference)             |             |
| A little                          | 39           | 0.90         | 0.43 - 1.85             |             | 30           | 1.56         | 0.55 - 4.42             |             |
| Fair                              | 210          | 1.14         | 0.58 - 2.21             |             | 115          | 1.80         | 0.66 - 4.88             |             |
| Pretty                            | 119          | 1.11         | 0.56 - 2.18             |             | 35           | 1.51         | 0.54 - 4.26             |             |
| Very much                         | 51           | 1.36         | 0.67 - 2.78             | 0.12        | 13           | 1.89         | 0.62 - 5.79             | 0.57        |

**Table 3.** Age-adjusted hazard ratios of stomach cancer for intake of meat, fish, and marine foods by sex.

|                          | Male         |              |                         |             | Female       |              |                         |             |
|--------------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                          | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Beef</b>              |              |              |                         |             |              |              |                         |             |
| None                     | 100          | 1.00         | (reference)             |             | 48           | 1.00         | (reference)             |             |
| 1-2/month                | 119          | 0.79         | 0.61 - 1.04             |             | 52           | 1.02         | 0.69 - 1.51             |             |
| 1-2/week                 | 92           | 0.73         | 0.55 - 0.96             |             | 51           | 1.09         | 0.74 - 1.62             |             |
| 3-4/week                 | 34           | 1.00         | 0.67 - 1.47             |             | 13           | 0.92         | 0.50 - 1.69             |             |
| 1+/day                   | 6            | 0.90         | 0.39 - 2.05             | 0.30        | 4            | 2.05         | 0.74 - 5.68             | 0.60        |
| <b>Pork</b>              |              |              |                         |             |              |              |                         |             |
| None                     | 40           | 1.00         | (reference)             |             | 26           | 1.00         | (reference)             |             |
| 1-2/month                | 84           | 0.96         | 0.66 - 1.41             |             | 40           | 1.13         | 0.69 - 1.85             |             |
| 1-2/week                 | 173          | 1.10         | 0.78 - 1.55             |             | 78           | 1.16         | 0.74 - 1.82             |             |
| 3-4/week                 | 66           | 1.10         | 0.74 - 1.62             |             | 34           | 1.35         | 0.81 - 2.26             |             |
| 1+/day                   | 14           | 1.05         | 0.57 - 1.93             | 0.45        | 7            | 1.50         | 0.65 - 3.48             | 0.21        |
| <b>Sausage</b>           |              |              |                         |             |              |              |                         |             |
| None                     | 108          | 1.00         | (reference)             |             | 54           | 1.00         | (reference)             |             |
| 1-2/month                | 101          | 0.93         | 0.71 - 1.22             |             | 54           | 1.31         | 0.90 - 1.91             |             |
| 1-2/week                 | 139          | 1.00         | 0.77 - 1.28             |             | 62           | 1.13         | 0.78 - 1.64             |             |
| 3-4/week                 | 71           | 1.24         | 0.92 - 1.67             |             | 26           | 1.18         | 0.74 - 1.89             |             |
| 1+/day                   | 20           | 1.36         | 0.85 - 2.20             | 0.10        | 9            | 1.82         | 0.90 - 3.70             | 0.27        |
| <b>Chicken</b>           |              |              |                         |             |              |              |                         |             |
| None                     | 54           | 1.00         | (reference)             |             | 18           | 1.00         | (reference)             |             |
| 1-2/month                | 99           | 0.62         | 0.45 - 0.86             |             | 50           | 1.12         | 0.66 - 1.93             |             |
| 1-2/week                 | 179          | 0.71         | 0.52 - 0.96             |             | 92           | 1.09         | 0.66 - 1.81             |             |
| 3-4/week                 | 81           | 0.84         | 0.59 - 1.18             |             | 46           | 1.30         | 0.76 - 2.25             |             |
| 1+/day                   | 12           | 0.73         | 0.39 - 1.37             | 0.98        | 7            | 1.33         | 0.55 - 3.17             | 0.33        |
| <b>Liver</b>             |              |              |                         |             |              |              |                         |             |
| None                     | 173          | 1.00         | (reference)             |             | 81           | 1.00         | (reference)             |             |
| 1-2/month                | 114          | 0.84         | 0.66 - 1.06             |             | 56           | 1.26         | 0.90 - 1.78             |             |
| 1-2/week                 | 67           | 1.06         | 0.80 - 1.41             |             | 32           | 1.39         | 0.92 - 2.11             |             |
| 3-4/week                 | 22           | 1.27         | 0.82 - 1.99             |             | 13           | 2.02         | 1.12 - 3.63             |             |
| 1+/day                   | 2            | 0.56         | 0.14 - 2.28             | 0.75        | 4            | 3.16         | 1.16 - 8.62             | 0.00        |
| <b>Fish</b>              |              |              |                         |             |              |              |                         |             |
| 1-2/month or less        | 45           | 1.00         | (reference)             |             | 16           | 1.00         | (reference)             |             |
| 1-2/week                 | 144          | 0.85         | 0.61 - 1.19             |             | 65           | 1.22         | 0.71 - 2.11             |             |
| 3-4/week                 | 154          | 0.90         | 0.65 - 1.26             |             | 94           | 1.62         | 0.95 - 2.75             |             |
| 1+/day                   | 136          | 0.95         | 0.68 - 1.33             | 0.73        | 63           | 1.41         | 0.82 - 2.45             | 0.13        |
| <b>Boiled fish paste</b> |              |              |                         |             |              |              |                         |             |
| None                     | 75           | 1.00         | (reference)             |             | 32           | 1.00         | (reference)             |             |
| 1-2/month                | 107          | 1.03         | 0.77 - 1.38             |             | 43           | 0.91         | 0.58 - 1.44             |             |
| 1-2/week                 | 116          | 1.27         | 0.95 - 1.69             |             | 70           | 1.47         | 0.97 - 2.24             |             |
| 3-4/week or more         | 58           | 1.21         | 0.86 - 1.71             | 0.10        | 30           | 1.25         | 0.76 - 2.06             | 0.06        |
| <b>Seaweed</b>           |              |              |                         |             |              |              |                         |             |
| 1-2/month or less        | 59           | 1.00         | (reference)             |             | 22           | 1.00         | (reference)             |             |
| 1-2/week                 | 133          | 0.90         | 0.66 - 1.22             |             | 53           | 0.75         | 0.46 - 1.24             |             |
| 3-4/week                 | 176          | 1.15         | 0.86 - 1.55             |             | 79           | 0.90         | 0.56 - 1.44             |             |
| 1+/day                   | 158          | 1.04         | 0.77 - 1.40             | 0.29        | 103          | 0.97         | 0.61 - 1.54             | 0.38        |

**Table 4.** Age adjusted hazard ratios of stomach cancer for intake of daily products by sex.

|                   | Male         |              |                         |             | Female       |              |                         |             |
|-------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                   | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Egg</b>        |              |              |                         |             |              |              |                         |             |
| 1-2/month or less | 34           | 1.00         | (reference)             |             | 10           | 1.00         | (reference)             |             |
| 1-2/week          | 119          | 1.16         | 0.79 - 1.69             |             | 52           | 1.80         | 0.91 - 3.53             |             |
| 3-4/week          | 118          | 0.90         | 0.62 - 1.32             |             | 76           | 2.11         | 1.09 - 4.09             |             |
| 1+/day            | 260          | 1.13         | 0.79 - 1.62             | 0.64        | 124          | 2.32         | 1.22 - 4.42             | 0.01        |
| <b>Milk</b>       |              |              |                         |             |              |              |                         |             |
| None              | 100          | 1.00         | (reference)             |             | 60           | 1.00         | (reference)             |             |
| 1-2/month         | 41           | 1.13         | 0.79 - 1.63             |             | 11           | 0.62         | 0.33 - 1.18             |             |
| 1-2/week          | 75           | 1.17         | 0.87 - 1.58             |             | 32           | 0.90         | 0.58 - 1.38             |             |
| 3-4/week          | 66           | 1.08         | 0.79 - 1.48             |             | 30           | 0.78         | 0.50 - 1.21             |             |
| 1+/day            | 223          | 1.06         | 0.84 - 1.35             | 0.81        | 115          | 0.83         | 0.60 - 1.13             | 0.34        |
| <b>Yogurt</b>     |              |              |                         |             |              |              |                         |             |
| None              | 247          | 1.00         | (reference)             |             | 100          | 1.00         | (reference)             |             |
| 1-2/month         | 35           | 0.69         | 0.49 - 0.98             |             | 29           | 0.95         | 0.63 - 1.43             |             |
| 1-2/week          | 28           | 0.86         | 0.58 - 1.28             |             | 33           | 1.38         | 0.93 - 2.05             |             |
| 3-4/week          | 18           | 1.22         | 0.76 - 1.97             |             | 10           | 0.85         | 0.44 - 1.63             |             |
| 1+/day            | 16           | 0.82         | 0.50 - 1.37             | 0.47        | 11           | 0.88         | 0.47 - 1.64             | 0.93        |
| <b>Cheese</b>     |              |              |                         |             |              |              |                         |             |
| None              | 191          | 1.00         | (reference)             |             | 106          | 1.00         | (reference)             |             |
| 1-2/month         | 82           | 0.93         | 0.72 - 1.20             |             | 47           | 1.31         | 0.92 - 1.85             |             |
| 1-2/week          | 51           | 1.08         | 0.80 - 1.48             |             | 19           | 0.93         | 0.57 - 1.52             |             |
| 3-4/week          | 23           | 1.32         | 0.86 - 2.04             |             | 5            | 0.60         | 0.24 - 1.46             |             |
| 1+/day            | 8            | 0.79         | 0.39 - 1.61             | 0.64        | 6            | 1.18         | 0.52 - 2.69             | 0.80        |
| <b>Butter</b>     |              |              |                         |             |              |              |                         |             |
| None              | 190          | 1.00         | (reference)             |             | 104          | 1.00         | (reference)             |             |
| 1-2/month         | 78           | 0.97         | 0.75 - 1.27             |             | 27           | 0.76         | 0.50 - 1.17             |             |
| 1-2/week          | 47           | 0.96         | 0.70 - 1.33             |             | 31           | 1.27         | 0.85 - 1.90             |             |
| 3-4/week          | 19           | 0.92         | 0.57 - 1.47             |             | 4            | 0.37         | 0.14 - 1.01             |             |
| 1+/day            | 11           | 0.70         | 0.38 - 1.29             | 0.33        | 11           | 1.22         | 0.65 - 2.26             | 0.89        |
| <b>Margarine</b>  |              |              |                         |             |              |              |                         |             |
| None              | 195          | 1.00         | (reference)             |             | 89           | 1.00         | (reference)             |             |
| 1-2/month         | 54           | 0.83         | 0.61 - 1.12             |             | 29           | 0.98         | 0.64 - 1.50             |             |
| 1-2/week          | 71           | 1.14         | 0.87 - 1.49             |             | 39           | 1.09         | 0.74 - 1.59             |             |
| 3-4/week          | 29           | 0.92         | 0.62 - 1.36             |             | 14           | 0.69         | 0.39 - 1.22             |             |
| 1+/day            | 25           | 0.72         | 0.48 - 1.10             | 0.36        | 20           | 0.82         | 0.50 - 1.33             | 0.30        |

**Table 5.** Age adjusted hazard ratios of stomach cancer for intake of starch food and style of breakfast by sex.

|                                 | Male         |              |                         |             | Female       |              |                         |             |
|---------------------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                                 | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Rice (cup)</b>               |              |              |                         |             |              |              |                         |             |
| 1/day or less                   | 47           | 0.93         | 0.68 - 1.28             |             | 36           | 1.25         | 0.86 - 1.80             |             |
| 2/day                           | 96           | 1.09         | 0.85 - 1.39             |             | 52           | 0.96         | 0.70 - 1.32             |             |
| 3/day                           | 198          | 1.00         | (reference)             |             | 132          | 1.00         | (reference)             |             |
| 4/day                           | 60           | 0.93         | 0.69 - 1.24             |             | 18           | 0.96         | 0.58 - 1.57             |             |
| 5/day                           | 69           | 1.05         | 0.80 - 1.38             |             | 18           | 1.31         | 0.80 - 2.15             |             |
| 6+/day                          | 69           | 0.97         | 0.74 - 1.28             | 0.87        | 8            | 0.75         | 0.37 - 1.54             | 0.54        |
| <b>Rice (cup) (thirties)</b>    |              |              |                         |             |              |              |                         |             |
| 1/day or less                   | 7            | 1.38         | 0.63 - 3.01             |             | 8            | 1.91         | 0.89 - 4.08             |             |
| 2/day                           | 36           | 0.87         | 0.58 - 1.32             |             | 26           | 1.09         | 0.66 - 1.79             |             |
| 3/day                           | 59           | 1.00         | (reference)             |             | 39           | 1.00         | (reference)             |             |
| 4/day                           | 35           | 1.15         | 0.76 - 1.75             |             | 23           | 1.21         | 0.72 - 2.03             |             |
| 5/day                           | 54           | 1.09         | 0.75 - 1.57             |             | 26           | 0.96         | 0.58 - 1.58             |             |
| 6+/day                          | 215          | 1.08         | 0.81 - 1.44             | 0.42        | 87           | 1.18         | 0.80 - 1.72             | 0.99        |
| <b>Potato</b>                   |              |              |                         |             |              |              |                         |             |
| 1-2/month or less               | 96           | 1.00         | (reference)             |             | 36           | 1.00         | (reference)             |             |
| 1-2/week                        | 181          | 1.08         | 0.84 - 1.38             |             | 67           | 0.66         | 0.44 - 0.98             |             |
| 3-4/week                        | 146          | 1.06         | 0.82 - 1.38             |             | 91           | 0.85         | 0.58 - 1.26             |             |
| 1+/day                          | 94           | 1.08         | 0.81 - 1.44             | 0.65        | 61           | 0.86         | 0.57 - 1.29             | 0.74        |
| <b>Japanese style breakfast</b> |              |              |                         |             |              |              |                         |             |
| No                              | 55           | 1.00         | (reference)             |             | 36           | 1.00         | (reference)             |             |
| Yes                             | 397          | 1.30         | 0.98 - 1.72             |             | 184          | 1.24         | 0.87 - 1.77             |             |
| <b>Western style breakfast</b>  |              |              |                         |             |              |              |                         |             |
| No                              | 418          | 1.00         | (reference)             |             | 182          | 1.00         | (reference)             |             |
| Yes                             | 34           | 0.49         | 0.35 - 0.70             |             | 38           | 0.82         | 0.58 - 1.17             |             |
| <b>Tea gruel for breakfast</b>  |              |              |                         |             |              |              |                         |             |
| No                              | 396          | 1.00         | (reference)             |             | 198          | 1.00         | (reference)             |             |
| Yes                             | 29           | 1.50         | 1.03 - 2.18             |             | 5            | 0.50         | 0.21 - 1.22             |             |

**Table 6.** Age adjusted hazard ratios of stomach cancer for intake of coffee and tea by sex.

|                        | Male         |              |                         |             | Female       |              |                         |             |
|------------------------|--------------|--------------|-------------------------|-------------|--------------|--------------|-------------------------|-------------|
|                        | No. of death | Hazard ratio | 95% confidence interval | p for trend | No. of death | Hazard ratio | 95% confidence interval | p for trend |
| <b>Coffee (cup)</b>    |              |              |                         |             |              |              |                         |             |
| None                   | 151          | 1.00         | (reference)             |             | 74           | 1.00         | (reference)             |             |
| 1-2/month              | 33           | 0.82         | 0.57 - 1.20             |             | 17           | 1.04         | 0.62 - 1.77             |             |
| 1-2/week               | 84           | 0.92         | 0.70 - 1.20             |             | 36           | 0.99         | 0.66 - 1.48             |             |
| 3-4/week               | 46           | 1.00         | 0.72 - 1.40             |             | 26           | 1.70         | 1.09 - 2.67             |             |
| 1+/day                 | 222          | 0.81         | 0.65 - 0.99             | 0.07        | 105          | 1.00         | 0.74 - 1.35             | 0.81        |
| <b>Coffee (cup)</b>    |              |              |                         |             |              |              |                         |             |
| 2/week or less         | 268          | 1.00         | (reference)             |             | 127          | 1.00         | (reference)             |             |
| less than 1/day        | 46           | 1.05         | 0.77 - 1.44             |             | 26           | 1.66         | 1.09 - 2.54             |             |
| 1/day                  | 45           | 0.82         | 0.60 - 1.12             |             | 30           | 1.03         | 0.69 - 1.54             |             |
| 2/day                  | 22           | 0.55         | 0.36 - 0.86             |             | 16           | 1.09         | 0.64 - 1.84             |             |
| 3+/day                 | 26           | 1.00         | 0.66 - 1.50             | 0.06        | 3            | 0.47         | 0.15 - 1.50             | 0.79        |
| <b>Black tea (cup)</b> |              |              |                         |             |              |              |                         |             |
| None                   | 308          | 1.00         | (reference)             |             | 154          | 1.00         | (reference)             |             |
| 1-2/month              | 48           | 0.98         | 0.72 - 1.33             |             | 20           | 0.75         | 0.47 - 1.20             |             |
| 1-2/week               | 20           | 0.75         | 0.48 - 1.18             |             | 13           | 0.82         | 0.46 - 1.44             |             |
| 3-4/week or more       | 32           | 1.41         | 0.98 - 2.03             | 0.29        | 14           | 1.03         | 0.60 - 1.79             | 0.84        |
| <b>China tea</b>       |              |              |                         |             |              |              |                         |             |
| less than 1/day        | 350          | 1.00         | (reference)             |             | 174          | 1.00         | (reference)             |             |
| 1+/day                 | 11           | 0.70         | 0.38 - 1.27             | 0.72        | 8            | 0.58         | 0.28 - 1.17             | 0.18        |

females (HR=1.54, 95% CI: 1.03-2.28).

The consumption of high salt foods such as miso soup, pickles, and dried fish was not significantly associated with the mortality of stomach cancer in males (Table 2). The relative risks of these foods were close to one. In females, the intake of pickles, fish boiled in soy sauce and strong taste of salty food elevated the risk of stomach cancer, but not significantly.

Table 3 shows the relationship between intake of meat, fish and marine foods, and stomach cancer. In males, those who had beef once or twice a week showed a significant decreased risk compared to those who hardly ever consumed beef (HR=0.73, 95% CI: 0.55-0.96). Regarding the intake of chicken, the relative risk of eating it once or twice a month was also significantly reduced (HR=0.62, 95% CI: 0.45-0.86). However, the association of meat, which included sausage and liver, with stomach cancer was not observed in males. On the other hand, those who consumed liver three to four times per week and more than once a day had a increased risk among females, respectively (RR=2.02, 95% CI: 1.12-3.63, RR=3.16, 95% CI: 1.16-8.62). The non-significantly higher risk for stomach cancer was found in the third highest consumption of fish (HR=1.62, 95% CI: 0.95-2.75). No clear association was found between the intake of other meat and fish and the risk of stomach cancer in females.

Men who had consumed yogurt once or twice a month showed a significant decreased risk compared to those who had hardly ever consumed yogurt (HR=0.69, 95% CI: 0.49-0.98) (Table 4). Daily products such as eggs and milk were not associated with stomach cancer in males. The relative risks for the second to quintile were close to null value. For intake of eggs among females, the relative risks for third and quartile significantly increased (HR=2.11, 95% CI: 1.09-4.09, HR=2.32, 95% CI: 1.22-4.42, respectively). Meantime, butter intake had a non-significant inverse association with stomach cancer risk (HR=0.37, 95% CI: 0.14-1.01).

Table 5 presented the relative risk of stomach cancer for starch food and style of breakfast. No significant association of rice intake with stomach cancer at present or in the thirties was observed in both males and females. Regarding the intake of potatoes once or twice a week in females, the relative risk significantly decreased (HR=0.66, 95% CI: 0.44-0.98). A western style breakfast showed a preventive association with stomach cancer in males (HR=0.49, 95% CI: 0.35-0.70). In contrast, tea gruel significantly elevated the risk of stomach cancer in males (HR=1.50, 95% CI: 1.03-2.18).

Coffee consumption showed a significant inverse association with the risk of stomach cancer in age-adjusted analysis among males, with a relative risk of 0.81 for the fifth intake category (more than one cup per day) (Table 6). However, the relative risk for the consumption of three or four cups of coffee per day was statistical significant in comparison with non-drinkers in females (HR=1.70, 95% CI: 1.09-2.67). Compared to those who drank less than two cups of coffee per week, women who drank three cups or more of coffee per week had an increased risk of stomach

cancer (HR=1.66, 95% CI: 1.09-2.54). There was no clear association between levels of consumption of coffee and the risk of stomach cancer among male.

## DISCUSSION

In this study, we found no association between stomach cancer mortality and the consumption of fruits and vegetables. The protective effect against stomach cancer of the consumption of a wide range of fruits and vegetables has been examined in epidemiological studies. Many case control studies have shown a decreased risk with fruits and vegetables,<sup>5-8</sup> although there are exceptions.<sup>11,18</sup> This protective effect might be due to food rich in vitamin C, such as oranges, tomatoes, citrus fruits. Vitamin C can prevent the formation of N-nitroso compounds.<sup>19,20</sup> In some studies, dietary intakes of micronutrients have been estimated. These studies have shown a consistent negative association of dietary intakes of vitamin C and carotenoids with stomach cancer.<sup>21-23</sup> In contrast, a negative association between the intakes of vegetables and fruits and stomach cancer has been less pronounced in limited cohort studies.<sup>24</sup> In some cohort studies, the intakes of micronutrients such as vitamin C,  $\beta$ -carotene, and other carotenes have been examined.<sup>16,25,26</sup> There was no significant difference in any micronutrients between men developing stomach cancer and those without stomach cancer. A meta-analytic approach to examine the evidence from cohort studies on total vegetable and fruit intake showed no significant protective effects.<sup>27</sup> In the meantime, an intervention trial using supplementation with  $\beta$ -carotene, vitamin E, and selenium showed reductions in stomach cancer mortality.<sup>28</sup> These results are difficult to generalize for populations who do not take supplements everyday.<sup>24</sup> In this study, consumption of liver was related to the high risk of stomach cancer in females. The reason for this association might be that women who often consume liver have suffered from anemia due to a stomach disorder including stomach cancer.

No salty food such as miso soup, pickled vegetable, and salted or dried fish was associated with the risk of stomach cancer. It has been suggested that salt intake is strongly associated with intestinal metaplasia and potentiates the effects of carcinogens.<sup>29</sup> In support of this hypothesis, several epidemiological studies have reported significant association between salt intake or salt attitude and stomach cancer,<sup>10,12,22</sup> but these are not universal findings.<sup>25,30,31</sup> Part of the reason for these discrepant results is that the intake of sodium is difficult to quantify.<sup>4</sup> To obtain a valid estimation of salt intake, rigorous dietary intake methodology, including information on discretionary use of table salt and soy sauce or direct measures of salt metabolism should be used. In this study, a food frequency questionnaire without portion size was used. Therefore, the relation between salt intake and stomach cancer risk may not be adequately appraised by this method.

Previous case control studies have not found any significant associations between the consumption of coffee with stomach cancer risk.<sup>7,31-34</sup> Coffee consumption showed a significant inverse



association with the risk of stomach cancer in males. Men who had a western style breakfast have a significant lower risk of stomach cancer. Coffee consumption is considered to be a westernized dietary habit. Mutagenic substances have been found in coffee,<sup>35-37</sup> although caffeine is not thought to be carcinogenic in humans when consumed in normal amounts.<sup>7</sup> However, we failed to observe a clear dose-response relationship between coffee consumption and stomach cancer risk. In addition, the intake of coffee increased the risk of stomach cancer in females. Therefore, this contradictory association between coffee consumption and stomach cancer in males and females needs further investigation.

Intakes of beef, chicken and yogurt in males, and potatoes in females showed a significantly decreased risk. However, this trend did not indicate a significant association. Frequencies of intakes of these foods were rather low, once or twice per week or month. These results suggested the necessity of further epidemiological studies to verify the association between these foods and risk of stomach cancer.

It is not certain why the present study did not find a significant association between the intake of foods and stomach cancer, as shown in the past cohort studies. The possibility exists that the food frequency questionnaire used in this study was not sensitive enough to detect meaningful differences in dietary intake due to the small number of food items (33 foods). The present study did not specifically include a number of other food items that have been positively related to stomach cancer in past studies, such as foods rich in nitrate-related compounds. We were not able to adjust for total calories, because a quantitative estimate of food consumption was not available. In addition, even if some foods showed the association with stomach cancer risk in this study, most of the association did not indicate a dose-response relationship. Therefore, it is important to carefully consider the results.

We have studied the association between the consumption of different foods and stomach cancer deaths. Subjects with subclinical stomach cancer may have changed their diet because of symptoms. We should also consider the possibility that the results of the present study based on mortality data reflected not causal factors, but prognostic factors of stomach cancer.

In conclusion, no clear association with individual food consumption was observed, although the results from this prospective study indicate that some foods were associated with stomach cancer risk. We also collected incidence cases of stomach cancer in this cohort. Further study will be required to use these data.

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