tality, but their sample sizes were small and the results were inconsistent.

We therefore designed this prospective analysis to examine the association between green tea consumption and mortality due to all causes, CVD, and cancer within a large population-based cohort study of 40 530 persons in Miyagi Prefecture in northeastern Japan, where green tea is widely consumed. Within this region, 80% of the population drinks green tea and more than half of them consume 3 or more cups/d.[12]

## METHODS

### Study Cohort

The details of the Ohsaki National Health Insurance (NHI) Cohort Study have been described in previous reports.[13-15] In brief, we delivered a self-administered questionnaire, including items on dietary intake (a 40-item food frequency questionnaire [FFQ]), between October and December 1994 to all NHI beneficiaries aged 40 to 79 years living in the catchment area of Ohsaki Public Health Center, Miyagi Prefecture, in northeastern Japan. Ohsaki Public Health Center, a local government agency, provides preventive health services for residents of 14 municipalities in Miyagi Prefecture. Of 54 996 eligible individuals, 52 029 (95%) responded.

To ascertain the date of and reason for withdrawal from the NHI, we started the prospective collection of NHI withdrawal history files on January 1, 1995. We excluded 774 participants who had withdrawn from the NHI before the baseline questionnaire survey. Thus, 51 255 participants ultimately formed the study cohort. The study protocol was reviewed and approved by the ethics committee of Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the participants to imply their consent to participate in the study.

For current analysis, we excluded participants who died before the collection of NHI withdrawal history files (n = 37) and those with missing data on green tea consumption frequency (n = 6821), as well as those who reported extreme daily energy intake (n = 444; sex-specific cutoffs for upper 0.5%, 3573.5 kcal/d for men and 2289.0 kcal/d for women; for lower 0.5%, 350.5 kcal/d for men and 200.0 kcal/d for women). We also excluded participants who reported a baseline history of cancer (n = 1481), myocardial infarction (n = 1149), or stroke (n = 793), since the presence of these diseases at baseline could have affected their diet and lifestyle. Consequently, our analysis involved 40 530 participants.

### Exposure Data

The questionnaire included items about the frequency of recent average consumption of 4 beverages (green tea, oolong tea, black tea, and coffee) and 36 items about food, as well as items regarding the consumption of alcohol and tobacco, personal and family history of disease, job status, level of education, body weight, height, engaging in sports or exercise, and time spent walking per day. The FFQ did not cover a specific period of time but asked about "everyday diet." The frequency of green tea consumption was divided into 5 categories: never, occasional, 1 to 2 cups/d, 3 to 4 cups/d, and 5 or more cups/d. Within the study region, the volume of a typical cup of green tea is 100 mL.

We conducted a validation study of the FFQ, in which 113 participants provided four 3-day food records within a period of 1 year and subsequently responded to the questionnaire. The results showed that the Spearman rank coefficient for the correlation between the amounts of green tea consumed according to the questionnaire and the amounts consumed according to the food records was 0.71 for men and 0.53 for women; the correlation between consumption measured by the 2 questionnaires administered 1 year apart was 0.63 for men and 0.64 for women.[16]

Because only 7% of the participants said they never drank green tea and only 19% said they drank it only occasionally, data from these respondents were collapsed into the single category of less than 1 cup/d for the purpose of this analysis. We examined the daily consumption of 40 food items, total energy, and nutrients from the FFQ responses by converting the selected frequency category for each food to a daily intake, using portion sizes based on the median values observed in four 3-day diet records. The FFQ used in this study has a high reproducibility and reasonably good validity in assessing the usual levels of intake of nutrients, foods, and food groups among our study population.[16]

### Follow-up

The end points were all-cause mortality and cause-specific mortality. To follow up the participants for mortality and migration, we reviewed the NHI withdrawal history files. When a participant was withdrawn from the NHI system because of death, emigration, or employment, the date of withdrawal and its reason were coded on the NHI withdrawal history files. Because we were unable to obtain subsequent information on the participants who withdrew from the NHI, we discontinued follow-up of participants who withdrew from the NHI system because of emigration or employment.

For decedents identified as described herein, we investigated cause of death by reviewing the death certificates filed at Ohsaki Public Health Center. Cause of death was coded by trained physicians according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (*ICD-10*).[17] We identified deaths from CVD as *ICD-10* codes I00-I99, coronary heart disease as *ICD-10* codes I20-I25, stroke as *ICD-10* codes I60-I69, cerebral infarction as *ICD-10* code I63, cerebral hemorrhage as *ICD-10* code I61, subarachnoid hemorrhage as *ICD-10* code I60, cancer as *ICD-10* codes C00-C97, gastric cancer as *ICD-10* code C16, lung cancer as *ICD-10* code C34, and colorectal cancer as *ICD-10* codes C18-C21. None of the participants died of unknown causes. Because the Family Registration Law in Japan requires registration of death, death certificates confirmed all deaths that occurred in the study area, except participants who died after emigration from the area.

### Statistical Analysis

For all-cause mortality, from January 1, 1995, to December 31, 2005, we prospectively counted the number of person-years of follow-up for each participant, from the beginning of follow-up until the date of death, the date of withdrawal from the NHI, or the end of follow-up, whichever occurred first. For cause-specific mortality, we followed up the participants for up to 7 years (1995-2001). The difference in follow-up times for all-cause mortality and cause-specific mortality results from the different sources of information. All-cause mortality data were obtained from the NHI withdrawal history files, which are provided every month and have no information on cause of death. Obtainment of cause-of-death data requires permission from the Japanese Ministry of Health, Labour, and Welfare to use the National Vital Statistics Database. Seven years of follow-up is the most up-to-date assessment of cause-of-death data in the study area as of August 1, 2006.

Cox proportional hazards regression analysis was used to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) of all-cause and cause-specific mortality according to green tea consumption categories and to adjust for potentially confounding variables, using SAS statistical software, version 9.1 (SAS Institute Inc, Cary, NC). For all models, the proportional hazards assumptions were tested and met through addition of time-dependent covariates to the models. Dummy variables were created for green tea consumption categories. The lowest category of green tea consumption was used as a reference category. The *P* values for the analysis of linear trends were calculated by scoring the categories, from 1 for the lowest category to 4 for the highest, entering the number as a continuous term in the regression model. In the analyses for oolong tea or black tea as a main exposure, individuals with missing data were excluded (n=9679 for oolong tea and n=10 140 for black tea).

We considered the following variables as potential confounders a priori: age at baseline (continuous variable), job status (employed or unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0),[18,19] engaging in sports or exercise (<1 h/wk, 1-2 h/wk, or ≥3 h/wk), time spent walking (<1 h/d or ≥1 h/d), history of hypertension (yes or no), history of diabetes mellitus (yes or no), history of gastric ulcer (yes or no), smoking status (never, former, currently smoking 1-19 cigarettes/d, or currently smoking ≥20 cigarettes/d), alcohol consumption (never, former, current ethanol intake of <45.6 g/d, or current ethanol intake of ≥45.6 g/d), daily total energy intake (continuous variable), daily rice consumption (<3 bowls, 3 bowls, 4 bowls, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, or coffee (never or occasionally, 1-2 cups/d, or ≥3 cups/d). To correct the estimates for socioeconomic status, the models were adjusted for job status and the number of years of education. In addition to engaging in sports or exercise, time spent walking was used as a measure of physical activity because it is the most common type of physical exercise among middle-aged and older individuals in rural Japan. The validity and reproducibility of the question on time spent walking has been reported elsewhere.[20] Alcohol consumption was classified in terms of *go*, a traditional Japanese unit of measure equal to approximately 180 mL of sake and containing 22.8 g of ethanol. Interactions between green tea consumption and confounders were tested through addition of cross-product terms to the multivariate model.

To minimize the possibility that diet or lifestyle factors had changed in response to subclinical disease, we repeated all analyses after excluding participants who had died in the first 3 years of follow-up. To ensure that the estimates were not biased by multicollinearity, the age- and sex-adjusted HRs for the green tea consumption categories were also calculated and compared with the multivariate adjusted HRs. All reported *P* values are 2-tailed, and the differences at $P<.05$ are considered statistically significant.

## RESULTS

Baseline characteristics of the participants by green tea consumption category are shown in TABLE 1 and TABLE 2. Participants who consumed green tea more often tended to be older and were more likely to be unemployed, to engage in sports or exercise, and to have a history of hypertension and diabetes mellitus and were less likely to walk, for both men and women. Men were also more likely to have a history of gastric ulcer and women to be obese. Men and women were both also more likely to consume individual foods or beverages such as miso (soybean paste) soup, soybean products, total fish, dairy products, total fruits, total vegetables, oolong tea, and black tea, but less likely to consume coffee. There were no apparent associations between smoking status or alcohol drinking and green tea consumption categories.

Over 11 years of follow-up, among 374 174 accrued person-years, the total number of deaths was 4209. The follow-up rate was 86.1%. TABLE 3 shows the association between green tea consumption and the HRs and associated 95% CIs of mortality due to all causes. We found that green tea consumption was inversely associated with mortality due to all causes and that the inverse association was more pronounced in women ($P=.03$ for

**Table 1.** Baseline Characteristics of Men According to Green Tea Consumption*

| Characteristics | Green Tea Consumption, Cups/d <br> <1 (n = 5801) | 1-2 (n = 4325) | 3-4 (n = 3895) | ≥5 (n = 5039) | *P* Value† |
|---|---|---|---|---|---|
| Age, mean (SD), y | 57.6 (10.7) | 57.8 (10.8) | 60.3 (10.3) | 61.8 (9.9) | <.001 |
| Job status | | | | | |
| Employed | 3844 (85.1) | 2904 (84.7) | 2476 (79.3) | 3129 (78.2) | <.001 |
| Unemployed | 673 (14.9) | 523 (15.3) | 647 (20.7) | 870 (21.8) | |
| Years of education | | | | | |
| <10 | 3475 (62.6) | 2366 (56.7) | 2212 (58.7) | 3017 (61.8) | <.001 |
| 10-12 | 1700 (30.6) | 1461 (35.0) | 1214 (32.2) | 1488 (30.5) | |
| ≥13 | 375 (6.8) | 346 (8.3) | 342 (9.1) | 374 (7.7) | |
| Body mass index‡ | | | | | |
| <18.5 | 179 (3.3) | 138 (3.3) | 99 (2.6) | 189 (3.9) | .007 |
| 18.5-22.9 | 2397 (43.5) | 1812 (43.8) | 1714 (45.6) | 2092 (43.2) | |
| 23.0-24.9 | 1446 (26.2) | 1125 (27.2) | 1004 (26.7) | 1356 (28.0) | |
| 25.0-29.9 | 1379 (25.0) | 967 (23.4) | 871 (23.2) | 1128 (23.3) | |
| ≥30.0 | 113 (2.1) | 92 (2.2) | 68 (1.8) | 76 (1.6) | |
| Sports/exercise, h/wk | | | | | |
| <1 | 3950 (73.0) | 2808 (69.5) | 2454 (67.4) | 3132 (66.7) | <.001 |
| 1-2 | 743 (13.7) | 655 (16.2) | 599 (16.5) | 712 (15.2) | |
| ≥3 | 717 (13.3) | 575 (14.2) | 589 (16.2) | 855 (18.2) | |
| Walking duration, h/d | | | | | |
| <1 | 2687 (49.9) | 2059 (50.8) | 1956 (53.6) | 2404 (51.1) | .006 |
| ≥1 | 2700 (50.1) | 1993 (49.2) | 1694 (46.4) | 2297 (48.9) | |
| History of hypertension | | | | | |
| Yes | 1240 (21.4) | 1001 (23.1) | 984 (25.3) | 1229 (24.4) | <.001 |
| No | 4561 (78.6) | 3324 (76.9) | 2911 (74.7) | 3810 (75.6) | |
| History of diabetes mellitus | | | | | |
| Yes | 392 (6.8) | 280 (6.5) | 305 (7.8) | 369 (7.3) | .07 |
| No | 5409 (93.2) | 4045 (93.5) | 3590 (92.2) | 4670 (92.7) | |
| History of gastric ulcer | | | | | |
| Yes | 1114 (19.2) | 851 (19.7) | 797 (20.5) | 1106 (22.0) | .003 |
| No | 4687 (80.8) | 3474 (80.3) | 3098 (79.5) | 3933 (78.1) | |
| Smoking status | | | | | |
| Never | 1150 (21.6) | 809 (20.4) | 719 (19.9) | 821 (17.6) | <.001 |
| Former | 1300 (24.4) | 963 (24.3) | 1018 (28.1) | 1330 (28.5) | |
| Current, <20 cigarettes/d | 927 (17.4) | 713 (18.0) | 647 (17.9) | 877 (18.8) | |
| Current, ≥20 cigarettes/d | 1943 (36.5) | 1478 (37.3) | 1236 (34.1) | 1632 (35.0) | |
| Alcohol drinking | | | | | |
| Never | 928 (16.8) | 608 (14.8) | 562 (15.1) | 905 (18.8) | <.001 |
| Former | 197 (3.6) | 119 (2.9) | 117 (3.1) | 171 (3.6) | |
| Current, <45.6 g/d ethanol | 4176 (75.8) | 3256 (79.2) | 2957 (79.4) | 3586 (74.6) | |
| Current, ≥45.6 g/d ethanol | 210 (3.8) | 129 (3.1) | 88 (2.4) | 144 (3.0) | |
| Total energy intake, mean (SD), kcal/d | 1783.5 (612.2) | 1812.8 (603.7) | 1852.2 (589.7) | 1905.0 (592.8) | <.001 |
| Daily dietary consumption | | | | | |
| Rice, ≥4 bowls | 1951 (34.0) | 1419 (33.1) | 1281 (33.3) | 1726 (34.7) | .34 |
| Miso (soybean paste) soup | 4933 (86.5) | 3819 (89.5) | 3506 (91.4) | 4581 (92.4) | <.001 |
| Soybean products, mean (SD), g | 46.5 (28.7) | 50.0 (28.3) | 52.7 (27.6) | 56.8 (27.0) | <.001 |
| Total meat, mean (SD), g | 22.5 (19.2) | 23.2 (18.6) | 22.9 (17.4) | 23.1 (18.9) | <.001 |
| Total fish, mean (SD), g | 55.2 (35.5) | 57.5 (34.8) | 61.2 (34.3) | 66.6 (34.7) | <.001 |
| Dairy products, mean (SD), g | 119.0 (98.9) | 127.8 (98.5) | 130.1 (98.8) | 134.6 (99.6) | <.001 |
| Total fruits, mean (SD), g | 63.6 (53.1) | 71.0 (54.9) | 77.8 (55.5) | 90.1 (58.3) | <.001 |
| Total vegetables, mean (SD), g | 61.8 (42.9) | 66.7 (43.1) | 72.4 (43.3) | 77.5 (46.0) | <.001 |
| Oolong tea, ≥3 cups/d | 181 (3.7) | 88 (2.7) | 99 (3.5) | 149 (4.1) | <.001 |
| Black tea, ≥3 cups/d | 20 (0.4) | 24 (0.8) | 48 (1.7) | 50 (1.4) | <.001 |
| Coffee, ≥3 cups/d | 798 (14.9) | 497 (13.3) | 370 (11.1) | 495 (11.8) | <.001 |

*Data are expressed as No. (%) unless otherwise indicated.
†*P* values calculated by analysis of variance or $\chi^2$ test.
‡Body mass index was calculated as weight in kilograms divided by height in meters squared.

**Table 2.** Baseline Characteristics of Women According to Green Tea Consumption*

| | Green Tea Consumption, Cups/d | | | | |
|---|---|---|---|---|---|
| Characteristics | <1 (n = 4901) | 1-2 (n = 4478) | 3-4 (n = 4944) | ≥5 (n = 7147) | *P* Value† |
| Age, mean (SD), y | 58.9 (10.8) | 60.1 (10.5) | 61.6 (9.7) | 62.7 (9.2) | <.001 |
| Job status | | | | | |
| Employed | 2086 (55.8) | 1842 (52.7) | 1710 (44.7) | 2319 (42.8) | <.001 |
| Unemployed | 1656 (44.3) | 1656 (47.3) | 2119 (55.3) | 3097 (57.2) | |
| Years of education | | | | | |
| <10 | 2709 (59.2) | 2303 (54.5) | 2558 (54.3) | 3949 (58.2) | <.001 |
| 10-12 | 1527 (33.4) | 1560 (36.9) | 1739 (36.9) | 2277 (33.5) | |
| ≥13 | 340 (7.4) | 366 (8.7) | 410 (8.7) | 564 (8.3) | |
| Body mass index‡ | | | | | |
| <18.5 | 211 (4.6) | 155 (3.6) | 190 (4.0) | 247 (3.6) | <.001 |
| 18.5-22.9 | 1856 (40.3) | 1697 (39.8) | 1924 (40.8) | 2579 (37.8) | |
| 23.0-24.9 | 1107 (24.1) | 1086 (25.5) | 1162 (24.6) | 1705 (25.0) | |
| 25.0-29.9 | 1244 (27.0) | 1194 (28.0) | 1286 (27.2) | 2031 (29.8) | |
| ≥30.0 | 183 (4.0) | 131 (3.1) | 159 (3.4) | 265 (3.9) | |
| Sports/exercise, h/wk | | | | | |
| <1 | 3376 (76.7) | 2917 (73.0) | 3144 (70.4) | 4656 (72.7) | <.001 |
| 1-2 | 586 (13.3) | 665 (16.7) | 784 (17.6) | 998 (15.6) | |
| ≥3 | 441 (10.0) | 413 (10.3) | 539 (12.1) | 753 (11.8) | |
| Walking duration, h/d | | | | | |
| <1 | 2454 (55.7) | 2315 (56.4) | 2659 (59.0) | 3794 (58.6) | .002 |
| ≥1 | 1952 (44.3) | 1793 (43.7) | 1847 (41.0) | 2686 (41.5) | |
| History of hypertension | | | | | |
| Yes | 1205 (24.6) | 1221 (27.3) | 1410 (28.5) | 2134 (29.9) | <.001 |
| No | 3696 (75.4) | 3257 (72.7) | 3534 (71.5) | 5013 (70.1) | |
| History of diabetes mellitus | | | | | |
| Yes | 252 (5.1) | 204 (4.6) | 262 (5.3) | 410 (5.7) | .05 |
| No | 4649 (94.9) | 4274 (95.4) | 4682 (94.7) | 6737 (94.3) | |
| History of gastric ulcer | | | | | |
| Yes | 531 (10.8) | 515 (11.5) | 547 (11.1) | 763 (10.7) | .56 |
| No | 4370 (89.2) | 3963 (88.5) | 4397 (88.9) | 6384 (89.3) | |
| Smoking status | | | | | |
| Never | 3380 (87.4) | 3239 (91.5) | 3649 (92.9) | 5008 (89.2) | <.001 |
| Former | 113 (2.9) | 84 (2.4) | 90 (2.3) | 151 (2.7) | |
| Current, <20 cigarettes/d | 238 (6.2) | 145 (4.1) | 142 (3.6) | 315 (5.6) | |
| Current, ≥20 cigarettes/d | 138 (3.6) | 73 (1.2) | 45 (1.2) | 142 (2.5) | |
| Alcohol drinking | | | | | |
| Never | 2883 (72.2) | 2707 (73.9) | 3071 (75.8) | 4297 (73.8) | <.001 |
| Former | 77 (1.9) | 43 (1.2) | 46 (1.1) | 80 (1.4) | |
| Current, <45.6 g/d ethanol | 1007 (25.2) | 903 (24.7) | 926 (22.9) | 1431 (24.6) | |
| Current, ≥45.6 g/d ethanol | 27 (0.7) | 8 (0.2) | 9 (0.2) | 15 (0.3) | |
| Total energy intake, mean (SD), kcal/d | 1188.3 (366.4) | 1231.3 (349.1) | 1268.9 (331.2) | 1310.2 (331.6) | <.001 |
| Daily dietary consumption | | | | | |
| Rice, ≥4 bowls | 507 (10.5) | 380 (8.6) | 403 (8.3) | 615 (8.7) | <.001 |
| Miso (soybean paste) soup | 4026 (84.0) | 3904 (88.9) | 4407 (90.5) | 6335 (90.4) | <.001 |
| Soybean products, mean (SD), g | 42.7 (24.3) | 46.9 (23.2) | 49.5 (22.0) | 51.1 (21.5) | <.001 |
| Total meat, mean (SD), g | 15.7 (14.1) | 16.0 (13.0) | 16.2 (12.5) | 16.3 (13.7) | .07 |
| Total fish, mean (SD), g | 47.2 (30.6) | 50.1 (30.4) | 53.6 (29.1) | 57.0 (29.8) | <.001 |
| Dairy products, mean (SD), g | 140.8 (102.3) | 151.3 (100.9) | 157.0 (100.0) | 155.0 (101.4) | <.001 |
| Total fruits, mean (SD), g | 96.9 (64.8) | 110.0 (64.0) | 119.1 (62.9) | 127.0 (63.3) | <.001 |
| Total vegetables, mean (SD), g | 71.5 (47.0) | 80.8 (47.3) | 84.9 (46.6) | 88.6 (48.4) | <.001 |
| Oolong tea, ≥3 cups/d | 311 (7.7) | 161 (4.9) | 231 (6.4) | 369 (7.1) | <.001 |
| Black tea, ≥3 cups/d | 17 (0.4) | 24 (0.8) | 40 (1.1) | 82 (1.6) | <.001 |
| Coffee, ≥3 cups/d | 550 (12.6) | 350 (9.2) | 308 (7.6) | 388 (6.7) | <.001 |

*Data are expressed as No. (%) unless otherwise indicated.
†*P* values calculated by analysis of variance or $\chi^2$ test.
‡Body mass index was calculated as weight in kilograms divided by height in meters squared.

interaction with sex). In men, the multivariate HRs of mortality due to all causes associated with different green tea consumption frequencies were 1.00 (reference) for less than 1 cup/d, 0.93 (95% CI, 0.83-1.05) for 1 to 2 cups/d, 0.95 (95% CI, 0.85-1.06) for 3 to 4 cups/d, and 0.88 (95% CI, 0.79-0.98) for 5 or more cups/d, respectively ($P=.03$ for trend). The corresponding data in women were 1.00, 0.98 (95% CI, 0.84-1.15), 0.82 (95% CI, 0.70-0.95), and 0.77 (95% CI, 0.67-0.89), respectively ($P<.001$ for trend). We included a variety of potential confounders in our multivariate models; however, the results did not change substantially even after adjustment for these variables. Comparison between the age- and sex-adjusted model and multivariate model suggested that the estimates were not biased by multicollinearity. When we excluded the 1018 participants who died in the first 3 years of follow-up, the results also did not change substantially.

Over 7 years of follow-up, among 252 101 total accrued person-years, the total number of deaths was 2931 (892 from CVD and 1134 from cancer). The follow-up rate was 89.6%. TABLE 4 shows the association between green tea consumption and the HRs and associated 95% CIs of mortality due to CVD and cancer. We found that green tea consumption was inversely associated with mortality due to CVD but not with that due to cancer. The inverse association with CVD mortality was stronger than that with all-cause mortality and the inverse association was also more pronounced in women ($P=.08$ for interaction with sex). In women, compared with those who consumed less than 1 cup/d of green tea, those who consumed 5 or more cups/d had a 31% lower risk of CVD death. In contrast, the association between green tea consumption and cancer mortality was substantially different. The HRs of cancer mortality were not significantly different from 1.00 in all green tea consumption categories compared with the lowest-consumption (referent) category.

We further investigated the association between green tea consumption and specific CVD and cancer mortality (TABLE 5, TABLE 6, and TABLE 7). In men, green tea consumption was significantly associated with reduced mortality due to stroke. In women, green tea consumption also was significantly associated with reduced mortality due to stroke, especially cerebral infarction. Compared with women who consumed less than 1 cup/d of green tea, those who consumed 5 or more cups/d had 42% and 62% lower risk of death due to stroke and cerebral infarction, respectively. In both men and women, the multivariate HRs of gastric, lung, and colorectal cancer mortality were mostly above unity but not statistically significant.

We conducted further stratified analyses of CVD mortality examining

**Table 3.** Cox Proportional Hazard Ratios (HRs) for 11-Year Mortality Due to All Causes by Green Tea Consumption in Japanese Adults

| | Green Tea Consumption, Cups/d | | | | |
|---|---|---|---|---|---|
| Mortality Outcomes | <1 | 1-2 | 3-4 | ≥5 | P Value for Trend |
| | | **Total Participants** | | | |
| No. of person-years | 97 127 | 80 416 | 82 121 | 114 510 | |
| No. of deaths | 1109 | 872 | 920 | 1308 | |
| Age- and sex-adjusted HR (95% CI) | 1.00 | 0.94 (0.86-1.03) | 0.88 (0.80-0.96) | 0.83 (0.77-0.90) | <.001 |
| Multivariate HR (95% CI)* | 1.00 | 0.96 (0.87-1.05) | 0.90 (0.82-0.98) | 0.84 (0.77-0.92) | <.001 |
| Multivariate HR (95% CI)† | 1.00 | 0.95 (0.85-1.05) | 0.92 (0.83-1.02) | 0.85 (0.77-0.94) | .001 |
| | | **Men** | | | |
| No. of person-years | 53 348 | 39 678 | 35 984 | 47 273 | |
| No. of deaths | 747 | 541 | 584 | 796 | |
| Age-adjusted HR (95% CI) | 1.00 | 0.96 (0.86-1.07) | 0.95 (0.86-1.06) | 0.89 (0.81-0.99) | .03 |
| Multivariate HR (95% CI)* | 1.00 | 0.93 (0.83-1.05) | 0.95 (0.85-1.06) | 0.88 (0.79-0.98) | .03 |
| Multivariate HR (95% CI)† | 1.00 | 0.94 (0.82-1.07) | 0.97 (0.85-1.10) | 0.88 (0.78-1.00) | .07 |
| | | **Women** | | | |
| No. of person-years | 43 779 | 40 738 | 46 137 | 67 238 | |
| No. of deaths | 362 | 331 | 336 | 512 | |
| Age-adjusted HR (95% CI) | 1.00 | 0.91 (0.78-1.05) | 0.75 (0.65-0.87) | 0.74 (0.64-0.84) | <.001 |
| Multivariate HR (95% CI)* | 1.00 | 0.98 (0.84-1.15) | 0.82 (0.70-0.95) | 0.77 (0.67-0.89) | <.001 |
| Multivariate HR (95% CI)† | 1.00 | 0.96 (0.81-1.15) | 0.86 (0.72-1.02) | 0.80 (0.68-0.94) | .003 |

Abbreviation: CI, confidence interval.

*The multivariate HR has been adjusted for age (continuous variable), sex (among total participants), job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d).

†Participants who died in the first 3 years of follow-up were excluded from this analysis.

subgroups defined by traditional CVD risk factors and dietary factors. The results in all subgroups showed the same inverse relationship between green tea consumption and CVD mortality, with no interactions noted. Although the interaction was not significant, the inverse association between green tea consumption and CVD mortality appeared to be more pronounced in participants who had never smoked. Among current smokers (n=11 614), the multivariate HRs of mortality due to CVD associated with different green tea consumption frequencies were 1.00 (reference) for less than 1 cup/d, 0.79 (95% CI, 0.55-1.14) for 1 to 2 cups/d, 0.81 (95% CI, 0.56-1.17) for 3 to 4 cups/d, and 0.86 (95% CI, 0.62-1.18) for 5 or more cups/d, respectively (*P*=.43 for trend). The corresponding data among never smokers (n=18 775) were 1.00, 0.85 (95% CI, 0.62-1.16), 0.69 (95% CI, 0.51-0.95), and 0.75 (95% CI, 0.56-1.00), respectively (*P*=.03 for trend).

**Table 4.** Cox Proportional Hazard Ratios (HRs) for 7-Year Mortality Due to Cardiovascular Disease and Cancer by Green Tea Consumption in Japanese Adults

| Mortality Outcomes | Green Tea Consumption, Cups/d | | | | *P* Value for Trend |
|---|---|---|---|---|---|
| | <1 | 1-2 | 3-4 | ≥5 | |
| **Total Participants** | | | | | |
| No. of person-years | 65656 | 54443 | 55290 | 76712 | |
| Cardiovascular disease mortality | | | | | |
| No. of deaths | 261 | 186 | 182 | 263 | |
| Age- and sex-adjusted HR (95% CI) | 1.00 | 0.83 (0.69-1.00) | 0.70 (0.58-0.85) | 0.67 (0.57-0.80) | <.001 |
| Multivariate HR (95% CI)* | 1.00 | 0.87 (0.72-1.06) | 0.77 (0.63-0.93) | 0.74 (0.62-0.89) | <.001 |
| Multivariate HR (95% CI)† | 1.00 | 0.76 (0.59-0.97) | 0.77 (0.60-0.98) | 0.74 (0.59-0.92) | .01 |
| Cancer mortality | | | | | |
| No. of deaths | 256 | 229 | 265 | 384 | |
| Age- and sex-adjusted HR (95% CI) | 1.00 | 1.08 (0.91-1.29) | 1.13 (0.95-1.34) | 1.11 (0.95-1.30) | .21 |
| Multivariate HR (95% CI)* | 1.00 | 1.11 (0.93-1.34) | 1.16 (0.97-1.38) | 1.11 (0.94-1.31) | .25 |
| Multivariate HR (95% CI)† | 1.00 | 1.12 (0.89-1.41) | 1.17 (0.94-1.46) | 1.11 (0.90-1.37) | .36 |
| **Men** | | | | | |
| No. of person-years | 36003 | 26885 | 24250 | 31718 | |
| Cardiovascular disease mortality | | | | | |
| No. of deaths | 149 | 103 | 98 | 131 | |
| Age-adjusted HR (95% CI) | 1.00 | 0.91 (0.71-1.17) | 0.79 (0.61-1.02) | 0.73 (0.58-0.92) | .005 |
| Multivariate HR (95% CI)* | 1.00 | 0.88 (0.68-1.14) | 0.84 (0.64-1.09) | 0.78 (0.61-1.00) | .06 |
| Multivariate HR (95% CI)† | 1.00 | 0.82 (0.59-1.16) | 0.91 (0.65-1.27) | 0.87 (0.64-1.19) | .49 |
| Cancer mortality | | | | | |
| No. of deaths | 179 | 142 | 175 | 243 | |
| Age-adjusted HR (95% CI) | 1.00 | 1.04 (0.84-1.30) | 1.21 (0.98-1.48) | 1.16 (0.96-1.41) | .08 |
| Multivariate HR (95% CI)* | 1.00 | 1.02 (0.82-1.28) | 1.18 (0.95-1.46) | 1.11 (0.90-1.36) | .22 |
| Multivariate HR (95% CI)† | 1.00 | 1.02 (0.77-1.35) | 1.13 (0.86-1.48) | 1.04 (0.80-1.35) | .66 |
| **Women** | | | | | |
| No. of person-years | 29653 | 27558 | 31040 | 44995 | |
| Cardiovascular disease mortality | | | | | |
| No. of deaths | 112 | 83 | 84 | 132 | |
| Age-adjusted HR (95% CI) | 1.00 | 0.74 (0.55-0.98) | 0.61 (0.46-0.81) | 0.62 (0.48-0.80) | <.001 |
| Multivariate HR (95% CI)* | 1.00 | 0.84 (0.63-1.12) | 0.69 (0.52-0.93) | 0.69 (0.53-0.90) | .004 |
| Multivariate HR (95% CI)† | 1.00 | 0.68 (0.47-0.98) | 0.65 (0.45-0.93) | 0.61 (0.44-0.85) | .006 |
| Cancer mortality | | | | | |
| No. of deaths | 77 | 87 | 90 | 141 | |
| Age-adjusted HR (95% CI) | 1.00 | 1.14 (0.84-1.55) | 0.97 (0.72-1.32) | 1.00 (0.75-1.32) | .68 |
| Multivariate HR (95% CI)* | 1.00 | 1.27 (0.93-1.74) | 1.09 (0.79-1.49) | 1.07 (0.80-1.44) | .97 |
| Multivariate HR (95% CI)† | 1.00 | 1.34 (0.90-1.98) | 1.22 (0.83-1.79) | 1.20 (0.83-1.73) | .53 |

Abbreviation: CI, confidence interval.

*The multivariate HR has been adjusted for age (continuous variable), sex (among total participants), job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d).

†Participants who died in the first 3 years of follow-up were excluded from this analysis.

The multivariate HRs of all-cause mortality according to green tea, oolong tea, and black tea consumption frequencies are compared in TABLE 8. Green tea consumption was associated with reduced mortality. In contrast, a weak or null association was observed between consumption of black tea or oolong tea and the HRs of all-cause mortality. We were unable to examine the associations between oolong tea or black tea and CVD or cancer mortality because of insufficient numbers of cases of disease among the higher-consumption categories of those beverages.

## COMMENT

On the basis of a large, population-based, prospective cohort study, we found significant inverse associations of green tea consumption with mortality due to all causes and due to CVD. Compared with participants who consumed less than 1 cup/d of green tea, those who consumed 5 or more cups/d had a risk of all-cause and CVD mortality that was 16% lower (during 11 years of follow-up) and 26% lower (during 7 years of follow-up), respectively. These inverse associations of all-cause and CVD mortality were primarily observed in women, although the inverse association for green tea consumption was observed in both sexes. In contrast, null results were observed in the association between green tea consumption and cancer mortality.

Sato et al[8] found a significant inverse association between green tea consumption and stroke mortality in 5910 participants over a 4-year period. Nakachi et al[9,11] reported an observed association between increased consumption of green tea and significantly lower risk of CVD death among 8552 individuals with a follow-up period of 11 to 13 years. Our findings were consistent with these results. In contrast, Iwai et al[10] did not observe significant association between green tea consumption and all-cause mortality, but the results were consistent with an inverse association between green tea consumption and all-cause mortality. The study had a much smaller sample size (2855 participants with 9.9 years of follow-up), and nonsignificant results might be due to low statistical power. Nakachi et al[9,11] also demonstrated that green tea consumption was associated with reduced mortality due to cancer, in contrast with our findings.

The reason for the discrepancy between men and women for the associa-

**Table 5.** Cox Proportional Hazard Ratios (HRs) Among All Participants for 7-Year Mortality Due to Cardiovascular Disease and Cancer Subtypes by Green Tea Consumption in Japanese Adults

| | Green Tea Consumption, Cups/d | | | | |
|---|---|---|---|---|---|
| Mortality Outcomes | <1 | 1-2 | 3-4 | ≥5 | *P* Value for Trend |
| Coronary heart disease | | | | | |
| No. of deaths | 58 | 47 | 43 | 61 | |
| Multivariate HR (95% CI)* | 1.00 | 1.04 (0.70-1.56) | 0.90 (0.60-1.36) | 0.86 (0.59-1.26) | .34 |
| Stroke | | | | | |
| No. of deaths | 145 | 99 | 102 | 126 | |
| Multivariate HR (95% CI)* | 1.00 | 0.84 (0.65-1.09) | 0.78 (0.60-1.01) | 0.63 (0.49-0.82) | <.001 |
| Cerebral infarction | | | | | |
| No. of deaths | 65 | 41 | 48 | 43 | |
| Multivariate HR (95% CI)* | 1.00 | 0.77 (0.52-1.15) | 0.81 (0.55-1.19) | 0.49 (0.33-0.73) | .001 |
| Cerebral hemorrhage | | | | | |
| No. of deaths | 34 | 30 | 33 | 40 | |
| Multivariate HR (95% CI)* | 1.00 | 1.10 (0.66-1.82) | 1.15 (0.70-1.89) | 0.98 (0.60-1.58) | .94 |
| Subarachnoid hemorrhage | | | | | |
| No. of deaths | 21 | 13 | 12 | 26 | |
| Multivariate HR (95% CI)* | 1.00 | 0.71 (0.35-1.44) | 0.57 (0.27-1.17) | 0.78 (0.42-1.43) | .42 |
| Gastric cancer | | | | | |
| No. of deaths | 44 | 44 | 38 | 67 | |
| Multivariate HR (95% CI)* | 1.00 | 1.33 (0.86-2.04) | 1.00 (0.64-1.58) | 1.17 (0.78-1.76) | .72 |
| Lung cancer | | | | | |
| No. of deaths | 49 | 41 | 46 | 82 | |
| Multivariate HR (95% CI)* | 1.00 | 1.03 (0.67-1.58) | 1.05 (0.69-1.59) | 1.18 (0.81-1.72) | .36 |
| Colorectal cancer | | | | | |
| No. of deaths | 30 | 24 | 36 | 42 | |
| Multivariate HR (95% CI)* | 1.00 | 1.04 (0.59-1.82) | 1.45 (0.87-2.41) | 1.10 (0.67-1.82) | .54 |

Abbreviation: CI, confidence interval.

*The multivariate HR has been adjusted for age (continuous variable), sex, job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared; <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d).

tions of green tea consumption and risk of all-cause and CVD mortality is uncertain. One possibility is the residual confounding by cigarette smoking. Men were more likely to smoke (Table 1 and Table 2), and the inverse associations between green tea consumption and CVD mortality appeared to be more pronounced in participants who had never smoked, although tests for interaction between green tea consumption categories and smoking in the analyses of CVD mortality yielded nonsignificant results. These results suggest that higher rates of smoking may mask the association of green tea consumption with CVD mortality among men.

Our finding of an inverse association between green tea consumption and CVD mortality appeared to be a threshold effect rather than a dose-response relationship, such that persons who consume at least 1 cup/d may receive some benefit. There may be differences in dietary intake and health characteristics besides green tea consumption between the lowest fourth and the highest three fourths of the distribution, suggesting that the observed association may be somehow explained by selection bias. However, in our models we adjusted for various potential confounders, and the estimates did not change substantially from the age- and sex-adjusted estimates.

Our results for CVD mortality may be partly explained by the effect of green tea on CVD risk profile. Previous studies have suggested that green tea may have beneficial effects on CVD risk profile, such as hypertension and obesity.[21,22] However, the present results of stratified analysis show that inverse associations were also evident among lean participants and among those who had no history of hypertension. Therefore, mechanisms other than the effects on traditional CVD risk factors might play a role. Green tea polyphenols, especially (-)-epigallocatechin-3-gallate, might explain the observed association with reduced all-cause and CVD mortality, irrespective of CVD risk profiles.[23,24] A number of biological mechanisms, including radical scavenging and antioxidant properties, have been proposed for the beneficial effects of green tea in different models of chronic disease.[3-6] The present inverse association between green tea consumption and cerebral infarction mortality, but not cerebral hemorrhage, indicates that green tea polyphenols

**Table 6.** Cox Proportional Hazard Ratios (HRs) Among Men for 7-Year Mortality Due to Cardiovascular Disease and Cancer Subtypes by Green Tea Consumption in Japanese Adults

| Mortality Outcomes | Green Tea Consumption, Cups/d | | | | *P* Value for Trend |
|---|---|---|---|---|---|
| | <1 | 1-2 | 3-4 | ≥5 | |
| Coronary heart disease | | | | | |
| No. of deaths | 37 | 29 | 27 | 36 | |
| Multivariate HR (95% CI)* | 1.00 | 1.03 (0.62-1.71) | 0.96 (0.57-1.62) | 0.91 (0.56-1.48) | .66 |
| Stroke | | | | | |
| No. of deaths | 79 | 53 | 59 | 58 | |
| Multivariate HR (95% CI)* | 1.00 | 0.85 (0.60-1.22) | 0.97 (0.68-1.37) | 0.65 (0.45-0.93) | .04 |
| Cerebral infarction | | | | | |
| No. of deaths | 37 | 23 | 33 | 23 | |
| Multivariate HR (95% CI)* | 1.00 | 0.78 (0.45-1.34) | 1.16 (0.71-1.91) | 0.58 (0.33-1.00) | .15 |
| Cerebral hemorrhage | | | | | |
| No. of deaths | 21 | 15 | 17 | 21 | |
| Multivariate HR (95% CI)* | 1.00 | 0.91 (0.46-1.78) | 1.08 (0.56-2.09) | 1.01 (0.53-1.91) | .88 |
| Subarachnoid hemorrhage | | | | | |
| No. of deaths | 10 | 5 | 3 | 5 | |
| Multivariate HR (95% CI)* | 1.00 | 0.58 (0.19-1.73) | 0.37 (0.10-1.38) | 0.37 (0.11-1.27) | .08 |
| Gastric cancer | | | | | |
| No. of deaths | 32 | 30 | 30 | 46 | |
| Multivariate HR (95% CI)* | 1.00 | 1.29 (0.78-2.16) | 1.19 (0.71-2.00) | 1.20 (0.74-1.95) | .55 |
| Lung cancer | | | | | |
| No. of deaths | 43 | 29 | 34 | 60 | |
| Multivariate HR (95% CI)* | 1.00 | 0.88 (0.54-1.42) | 0.97 (0.61-1.54) | 1.14 (0.75-1.73) | .46 |
| Colorectal cancer | | | | | |
| No. of deaths | 22 | 18 | 21 | 23 | |
| Multivariate HR (95% CI)* | 1.00 | 1.09 (0.57-2.09) | 1.23 (0.66-2.29) | 0.88 (0.47-1.63) | .74 |

Abbreviation: CI, confidence interval.

*The multivariate HR has been adjusted for age (continuous variable), job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared: <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d).

might directly affect atherosclerosis itself, irrespective of traditional CVD risk profiles.

We observed weak or null relationships between black tea or oolong tea and mortality. The discrepancy between green tea and other teas might indicate the specific role of substances rich in green tea. However, the smaller varia-

**Table 7.** Cox Proportional Hazard Ratios (HRs) Among Women for 7-Year Mortality Due to Cardiovascular Disease and Cancer Subtypes by Green Tea Consumption in Japanese Adults

| Mortality Outcomes | Green Tea Consumption, Cups/d <1 | 1-2 | 3-4 | ≥5 | *P* Value for Trend |
|---|---|---|---|---|---|
| Coronary heart disease | | | | | |
| No. of deaths | 21 | 18 | 16 | 25 | |
| Multivariate HR (95% CI)* | 1.00 | 1.04 (0.54-2.01) | 0.79 (0.40-1.56) | 0.77 (0.42-1.44) | .31 |
| Stroke | | | | | |
| No. of deaths | 66 | 46 | 43 | 68 | |
| Multivariate HR (95% CI)* | 1.00 | 0.79 (0.53-1.16) | 0.61 (0.41-0.90) | 0.58 (0.41-0.84) | .002 |
| Cerebral infarction | | | | | |
| No. of deaths | 28 | 18 | 15 | 20 | |
| Multivariate HR (95% CI)* | 1.00 | 0.76 (0.41-1.39) | 0.47 (0.24-0.89) | 0.38 (0.21-0.69) | <.001 |
| Cerebral hemorrhage | | | | | |
| No. of deaths | 13 | 15 | 16 | 19 | |
| Multivariate HR (95% CI)* | 1.00 | 1.33 (0.61-2.90) | 1.32 (0.61-2.82) | 0.98 (0.46-2.09) | .87 |
| Subarachnoid hemorrhage | | | | | |
| No. of deaths | 11 | 8 | 9 | 21 | |
| Multivariate HR (95% CI)* | 1.00 | 0.80 (0.32-2.03) | 0.71 (0.29-1.75) | 1.05 (0.49-2.26) | .81 |
| Gastric cancer | | | | | |
| No. of deaths | 12 | 14 | 8 | 21 | |
| Multivariate HR (95% CI)* | 1.00 | 1.32 (0.59-2.94) | 0.64 (0.26-1.63) | 1.08 (0.50-2.33) | .84 |
| Lung cancer | | | | | |
| No. of deaths | 6 | 12 | 12 | 22 | |
| Multivariate HR (95% CI)* | 1.00 | 1.83 (0.68-4.96) | 1.46 (0.54-3.95) | 1.59 (0.63-4.05) | .54 |
| Colorectal cancer | | | | | |
| No. of deaths | 8 | 6 | 15 | 19 | |
| Multivariate HR (95% CI)* | 1.00 | 0.98 (0.32-2.97) | 1.96 (0.78-4.95) | 1.49 (0.60-3.71) | .26 |

Abbreviation: CI, confidence interval.
*The multivariate HR has been adjusted for age (continuous variable), job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared: <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d).

**Table 8.** Cox Proportional Hazard Ratios (HRs) for 11-Year Mortality Due to All Causes by Type of Tea Consumption in Japanese Adults

| Mortality Outcomes | Tea Consumption, Cups/d <1 | 1-2 | ≥3 | *P* Value for Trend |
|---|---|---|---|---|
| Green tea | | | | |
| No. of person-years | 97 127 | 80 416 | 196 631 | |
| No. of deaths | 1109 | 872 | 2228 | |
| Multivariate HR (95% CI)* | 1.00 | 0.96 (0.87-1.06) | 0.87 (0.80-0.93) | <.001 |
| Oolong tea (Chinese tea) | | | | |
| No. of person-years | 256 266 | 15 909 | 14 715 | |
| No. of deaths | 2646 | 135 | 122 | |
| Multivariate HR (95% CI)* | 1.00 | 1.01 (0.84-1.21) | 1.03 (0.85-1.25) | .76 |
| Black tea | | | | |
| No. of person-years | 271 605 | 8313 | 2712 | |
| No. of deaths | 2750 | 87 | 33 | |
| Multivariate HR (95% CI)* | 1.00 | 1.00 (0.79-1.25) | 1.04 (0.72-1.51) | .89 |

Abbreviation: CI, confidence interval.
*The multivariate HR has been adjusted for age (continuous variable), sex, job status (employed vs unemployed), years of education (<10, 10-12, or ≥13), body mass index (calculated as weight in kilograms divided by height in meters squared: <18.5, 18.5-22.9, 23.0-24.9, 25.0-29.9, or ≥30.0), engaging in sports or exercise (<1, 1-2, or ≥3 h/wk), walking duration (<1 vs ≥1 h/d), history of hypertension, diabetes mellitus, and gastric ulcer (for each disease, yes or no), smoking status (never, former, currently smoking <20, or currently smoking ≥20 cigarettes/d), alcohol drinking (never, former, currently drinking <45.6 g/d, or currently drinking ≥45.6 g/d ethanol), total energy intake per day (continuous variable), daily consumption of rice (<3, 3, 4, or ≥5 bowls), daily consumption of miso (soybean paste) soup (yes or no), daily consumption of soybean products, total meat, total fish, dairy products, total fruits, and total vegetables (for each food, continuous variable), and consumption of green tea, oolong tea, black tea, and coffee (for each beverage, never or occasionally, 1-2 cups/d, or ≥3 cups/d). Models for green tea, oolong tea, or black tea did not include these variables, respectively.

 

tions in the consumption of black tea or oolong tea may have contributed in part to the noted lack of association with mortality.

Our study has limitations. First, the number of cases of individual CVD and cancer was only modest at best. Therefore, our study may not have had sufficient statistical power for detecting significant results in coronary heart disease or for detecting small increases or decreases in the risk of cancer at individual sites, as associated with green tea consumption. Second, 10.4% (during 7 years of follow-up) and 13.9% (during 11 years of follow-up) of total participants were lost to follow-up. However, this proportion did not vary across the green tea consumption categories (10.6%, 9.7%, 10.2%, and 10.8% of participants from the lowest to highest green tea consumption categories, respectively, were lost to follow-up during 7 years of follow-up, and 15.2%, 14.8%, 13.4%, and 12.4% of participants, respectively, were lost to follow-up during 11 years of follow-up). Therefore, we consider it unlikely that the association between green tea consumption and mortality was substantially distorted by the effect of loss to follow-up. Third, since green tea consumption was assessed on the basis on self-administered questionnaires, some misclassification of consumption status could arise in estimating the effect of the beverage. However, this misclassification may be nondifferential and would tend to result in underestimation of the impact of green tea consumption.

Healthy or unhealthy behavior, in association with high green tea consumption, could have confounded the correlation between green tea consumption and mortality. Almost all Japanese persons consume green tea as one of their favorite beverages and it is unlikely that green tea consumption was driven by health concerns. Therefore, the possibility that the observed inverse associations between green tea and mortality were confounded by habits related to health consciousness is small. However, although we statistically controlled for a variety of potential confounding factors and conducted analysis after excluding death during the first 3 years of follow-up, and the findings were robust, we could not eliminate residual confounding. Clinical trials are ultimately necessary to confirm the protective effect of green tea on mortality.

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CARDIOVASCULAR DISEASE

# Dietary patterns and cardiovascular disease mortality in Japan: a prospective cohort study

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**Background** Although ecological observations suggest that the Japanese diet may reduce the risk of cardiovascular disease (CVD), the impact of a Japanese dietary pattern upon mortality due to CVD is unclear.

**Methods** We prospectively assessed the association between dietary patterns among the Japanese and CVD mortality. Dietary information was collected from 40 547 Japanese men and women aged 40–79 years without a history of diabetes, stroke, myocardial infarction or cancer at the baseline in 1994.

**Results** During 7 years of follow-up, 801 participants died of CVD. Factor analysis (principal component) based on a validated food frequency questionnaire identified three dietary patterns: (i) a Japanese dietary pattern highly correlated with soybean products, fish, seaweeds, vegetables, fruits and green tea, (ii) an 'animal food' dietary pattern and (iii) a high-dairy, high-fruit-and-vegetable, low-alcohol (DFA) dietary pattern. The Japanese dietary pattern was related to high sodium intake and high prevalence of hypertension. After adjustment for potential confounders, the Japanese dietary pattern score was associated with a lower risk of CVD mortality (hazard ratio of the highest quartile vs the lowest, 0.73; 95% confidence interval: 0.59–0.90; $P$ for trend = 0.003). The 'animal food' dietary pattern was associated with an increased risk of CVD, but the DFA dietary pattern was not.

**Conclusion** The Japanese dietary pattern was associated with a decreased risk of CVD mortality, despite its relation to sodium intake and hypertension.

**Keywords** Diet, factor analysis, statistical, cardiovascular diseases, mortality, prospective studies, Japan

The traditional Japanese diet has drawn considerable attention since the 1960s because of its association with an extremely low rate of coronary heart disease (CHD).[1,2] On the other hand, this diet used to be characterized by high consumption of salt[2] and low consumption of animal fat and protein,[3] which would increase the risk of stroke, especially intracerebral haemorrhage (ICH).[4]

Over the past 40 years, however, the Japanese diet has changed. Average consumption of fruits, dairy products, eggs and meat has increased, while the high consumption of vegetables, soy products and fish has been maintained.[5] In parallel with the change from a traditional Japanese diet, the stroke mortality rate has fallen dramatically,[6] and the CHD mortality rate is still lower than in Western countries.[7] The age-adjusted rate of mortality due to cardiovascular disease (CVD) is lower than in the UK (~40%) and the US (~30%).[7] Thus, the contemporary Japanese diet may have beneficial effects in terms of lower CVD mortality.

While several single food items in the Japanese diet such as fish[8–10] and soybean[10,11] have been studied for CVD association, the results have not always been consistent. As food variables

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are highly intercorrelated and possibly have biochemical interactions, it is difficult to examine their separate effects.[12] To address the difficulties of the single food approach, many studies have investigated the association between dietary patterns and CVD among Western populations.[13–19]

Among the Japanese, previous studies on the association with specific cancers[20–22] or all-cause mortality[23] have identified a dietary pattern correlated with distinctive Japanese foods by using factor analysis.[24] However, no study has investigated the contribution of 'Japanese' dietary patterns to lower CVD mortality.

Our study objectives were to identify contemporary dietary patterns among the Japanese by factor analysis and to investigate their impact upon CVD mortality in a large-scale population-based prospective cohort study.

## Methods

### Study population

The details of the Ohsaki National Health Insurance (NHI) Cohort study have been described previously.[25,26] Briefly, we delivered a self-administered questionnaire including items on dietary intake [40-item food frequency questionnaire (FFQ)], medical history, smoking status and physical health status, between October and December 1994 to all NHI beneficiaries aged 40–79 years living in the catchment area of Ohsaki Public Health Center, Miyagi Prefecture, northeast Japan. Ohsaki Public Health Center, a local government agency, provides preventive health services for residents of 14 municipalities in Miyagi Prefecture. Of 54 996 eligible individuals, 52 029 (95.0%) responded.

From January 1, 1995, we started prospective collection of data on the date of death and withdrawal from the NHI, by obtaining NHI withdrawal history files from the local NHI Association. We excluded 774 participants because they had withdrawn from the NHI before collection of the NHI withdrawal history files. Thus, 51 255 participants formed the study cohort. The study protocol was reviewed and approved by the Ethics Committee of Tohoku University School of Medicine. We considered the return of self-administered questionnaires signed by the study participants to imply their consent to participate.

For current analysis, we excluded participants who died before collection of NHI withdrawal history files ($n = 37$), who left blank more than 24 of the 40 food items on the FFQ ($n = 3941$) and who reported daily energy intakes at the extreme 0.5% upper or lower ends of the range (sex-specific cut-off points were used: 1759 kJ, 14 884 kJ for men and 1256 kJ, 9609 kJ for women, respectively) ($n = 478$). We followed the exclusion criteria for the number of blanks on the FFQ reported in previous studies[17,18] of dietary patterns. We also excluded participants who reported a history of cancer ($n = 1533$), myocardial infarction ($n = 1325$), stroke ($n = 1040$) or diabetes mellitus at the baseline ($n = 3092$), because these diseases could have changed their diet and lifestyle. Consequently, our analysis included 40 547 participants.

### Dietary assessment

The 40-item FFQ asked about the average frequency of consumption of each food. Regarding the foods that showed different patterns of consumption between seasons, the FFQ asked about the frequency in the season when these foods were consumed most frequently within a year. However, the FFQ did not refer a specific time frame. Five frequency categories were used for the majority of food items (almost never, 1–2 days/month, 1–2 days/week, 3–4 days/week and almost every day). For rice and miso (fermented soybean paste) soup, the number of bowls consumed daily was asked. For current drinkers, the frequency of alcohol consumption was asked using four frequency categories (once or less/week, 1–2 days/week, 3–4 days/week, almost every day) and the usual amount was asked using six categories. For consumption of four non-alcohol beverages (green tea, black tea coffee and Chinese tea), five categories were used (almost never, sometimes, 1–2 cups/day, 3–4 cups/day, 5 or more cups/day).

We had previously conducted a validation study of the FFQ.[27] In brief, 113 participants (55 men and 58 women), who were a subsample of the cohort, provided four 3-day diet records (DRs) within a 1-year period and subsequently responded to the FFQ. We computed the Spearman correlation coefficients between the amounts consumed according to the DRs and the amounts consumed according to the FFQ. For 40 food items, medians (range) of the age and total energy-adjusted correlation coefficients were 0.35 (−0.30–0.72) in men and 0.34 (−0.06–0.75) in women. Medians (range) of the age and total energy-adjusted correlation coefficients of the two FFQs administered 1 year apart were 0.43 (0.14–0.76) in men and 0.45 (0.06–0.74) in women for the 40 food items.

We examined the daily consumption of 40 food items, total energy and nutrients from the FFQ by converting the selected frequency category for each food to a daily intake, using portion sizes based on the median values observed in the DRs. To calculate nutrients, we developed a food composition table that corresponded to the food items listed in the FFQ. Using the Standard Tables of Food Composition published by the Science and Technology Agency of Japan,[28] we calculated nutrients from the DRs and grouped the food codes to form food categories that best corresponded to the listing of the FFQ. We assigned relative weights to the food codes grouped into a single category based on the DR data.

### Dietary pattern derivation

To derive dietary patterns, factor analysis (principal component analysis) was conducted by using the daily consumption (weight in grams) of 40 food items from the FFQ. If the reported frequency was blank, we assumed that the item was never consumed. We used the PROC FACTOR procedure in SAS version 9.1[29] to perform the analyses. To determine the number of factors to retain, we considered eigenvalue, Scree test and factor interpretability.[24] Because 10 factors satisfied the criteria for eigenvalues greater than one, and the Scree plot indicated five factors that were retained, we selected solutions ranging from 2 to 5 for rotation. To achieve a simpler structure with greater interpretability, the factors were rotated by an orthogonal transformation (varimax rotation function in SAS).

With regard to factor interpretability, a three-factor solution appeared to describe most meaningfully the distinctive dietary patterns of the study population. We named them (i) a Japanese pattern, (ii) an 'animal food' pattern and (iii) a high-dairy, high-fruit-and-vegetable, and low-alcohol (DFA) pattern, according to the food items showing high factor loading (absolute value) with respect to each dietary pattern. These dietary patterns were consistent with those reported previously in Japanese men.[20] For each pattern and each participant, we calculated a factor score by summing the consumption from each food item weighted by its factor loading.[24]

We conducted additional sensitivity analysis of dietary pattern derivation. When we also performed factor analyses for six subgroups stratified by sex and three age groups (aged 40–59, 60–69 and 70–79 years), the derived patterns appeared similar. Thus, in our analyses, we used a factor solution including both men and women, and all age groups. Among the participants who left no blanks for food items ($n = 17010$), the derived dietary patterns closely resembled those derived from the total participants. As an additional analysis with stricter cut-off points of total energy intake for inclusion, we excluded participants who reported of daily energy intakes at the extreme 2.5% upper or lower ends of the range. The derived dietary patterns were similar to those of the main analysis.

Additional analyses using the maximum likelihood method instead of the principal component method as the initial factor-extracting method, and oblique rotation (promax rotation function in SAS) as a factor rotation method made the factor loadings for the three dietary patterns similar. The same criteria as the main analysis indicated three factors that were retained, and each factor was correlated to with (i) vegetables, fruits, seaweeds, soy products, and fish, (ii) meat and fat and (iii) rice (negatively), miso soup (negatively) and dairy products, respectively.

### Follow-up

The primary endpoint was CVD mortality. Secondarily, we conducted analyses of CHD and stroke mortality. We investigated cause of death by reviewing the death certificates filed at Ohsaki Public Health Center. Cause of death was coded by trained physicians according to the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10).[30] We identified deaths from CVD (codes I00-I99), CHD (codes I20-I25), total stroke (codes I60-I69), cerebral infarction (code I63) and ICH (code I61).

### Statistical analyses

From January 1, 1995 to December 31, 2001, we prospectively counted the number of person-years of follow-up for each participant from the beginning of follow-up until the date of death, withdrawal from the NHI or the end of the follow-up, whichever occurred first.

Cox proportional hazards regression analysis was used to calculate the hazard ratio (HR) and 95% confidence interval (CI) of CVD mortality according to quartiles of the dietary pattern score and to adjust for potentially confounding variables, using SAS.[29] For all models, the proportional hazards assumptions were tested and met using time-dependent covariates.[31] Dummy variables were created for the quartiles of each dietary pattern score. The lowest quartile of a dietary pattern score was used as a reference category. The $P$-values for analysis of linear trends were calculated by scoring the quartiles of a dietary pattern score, from one for the lowest quartile to four for the highest, entering the number as a continuous term in the regression model. Interaction between sex and quartiles of each dietary pattern score was tested by addition of cross-product terms to the multivariate model. The association between each dietary pattern and CVD mortality did not vary by sex ($P$ for interaction $n = 0.55$). All reported $P$-values are two-tailed.

Multivariate models were adjusted for the following variables: age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes per day and currently smoking $\geq$20 cigarettes per day), walking duration (<1 hour per day and $\geq$1 hour per day), total energy intake (as a continuous variable), body mass index (<18.5 kg/m$^2$, 18.5–24.9 kg/m$^2$ and $\geq$25.0 kg/m$^2$) and history of hypertension (yes or no). Two multivariate models not including and including body mass index and history of hypertension were used, since these two factors could be regarded as intermediate in the causal pathway between dietary pattern and CVD mortality. Walking duration was used as a parameter of physical activity because it is the most common type of physical activity among middle-aged and older individuals in rural Japan. The validity and reproducibility of the question on walking time has been reported elsewhere.[32]

All analyses were repeated after exclusion of participants who had died in the first 3 years of follow-up. To minimize any possible bias caused by physically inactive participants, we performed additional analysis that was restricted to participants who were able to perform vigorous activity [Medical Outcome Study (MOS) Short Form General Health Survey[33] score of 5–6] and with a well self-perceived health status. As an additional analysis, dietary pattern scores were adjusted for total energy by using the residual method.[34]

## Results

Table 1 shows factor loadings, which are equivalent to simple correlations between the food items and dietary patterns. A positive loading indicates that a food item is positively associated with the dietary pattern, and a negative loading indicates an inverse association with the dietary pattern. That is, food items highly loaded within a dietary pattern are highly correlated with each other.

The Japanese dietary pattern was loaded heavily on soybean products, fish, seaweeds, vegetables, fruits and green tea, whereas the 'animal food' pattern was loaded heavily on various animal-derived foods (beef, pork, ham, sausage, chicken, liver and butter), coffee and alcoholic beverages. The DFA dietary pattern was heavily loaded on dairy products (milk and yoghurt), margarine, fruits and vegetables (carrot, pumpkin and tomato), and negatively loaded on rice, miso soup and alcoholic beverages. These three dietary patterns explained 26.2% of the variance.

Table 2 compares the characteristics of participants according to the quartiles of each dietary pattern score. Participants

**Table 1** Factor-loading matrix for the major dietary pattern identified by factor analysis

| | Japanese pattern | 'Animal food' pattern | DFA[a] pattern |
|---|---|---|---|
| Rice | | | −0.59 |
| Miso soup | 0.25 | | −0.39 |
| Beef | | 0.48 | |
| Pork (excluding ham, sausage) | | 0.55 | |
| Ham, sausage | | 0.56 | |
| Chicken | | 0.49 | |
| Liver | | 0.43 | |
| Egg | 0.34 | 0.32 | |
| Milk | 0.26 | | 0.28 |
| Yoghurt | | | 0.50 |
| Cheeses | | 0.44 | |
| Butter | | 0.50 | |
| Margarine | | 0.37 | 0.40 |
| Deep fried-dishes, tempura | 0.28 | 0.39 | |
| Fried vegatable | 0.43 | | |
| Raw fish, fish boiled with soy, roast fish | 0.51 | | |
| Boiled fish paste | 0.39 | 0.32 | |
| Dried fish | 0.37 | | |
| Green vegetables | 0.64 | | |
| Carrot, pumpkin | 0.59 | | 0.36 |
| Tomato | 0.45 | | 0.32 |
| Cabbage, lettuce | 0.59 | | |
| Chinese cabbage | 0.62 | | |
| Wild plant | 0.27 | | |
| Mushrooms (shiitake, enokitake) | 0.42 | | |
| Potato | 0.61 | | |
| Seaweeds | 0.59 | | 0.26 |
| Pickles (radish, chinese cabbage) | 0.41 | | |
| Food boiled with soy | | | |
| Boiled beans | | | |
| Soybean (tofu, fermented soybeans) | 0.57 | | |
| Orange | 0.50 | | 0.42 |
| Other fruits | 0.49 | | 0.47 |
| Fresh juice | | | |
| Confectioneries | 0.27 | | |
| Green tea | 0.29 | | |
| Black tea | | | |
| Coffee | | 0.29 | |
| Chinese tea | | | |
| Alcoholic beverages | | 0.27 | −0.50 |
| Variance explained (%) | 15.1 | 6.4 | 4.8 |

[a] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.
Absolute values <0.25 were not listed for simplicity.

with a higher Japanese dietary pattern score tended to be older, were more likely to walk and have a history of hypertension, and less likely to be current drinkers and smokers. Participants with a higher 'animal food' dietary pattern score tended to be younger and male, were more likely to be current smokers and drinkers, and less likely to have a history of hypertension. Participants with a higher DFA dietary pattern score tended to be female, and were similar to those with a higher Japanese dietary pattern score except for walking duration, education and history of hypertension.

Table 3 shows total energy-adjusted daily nutrient and food intakes according to dietary pattern score quartiles. Although the fat and protein intakes in any given quintile of dietary patterns were almost equivalent, their sources varied among dietary patterns. Participants with a higher Japanese dietary pattern score consumed more fish and soybean, a higher 'animal food' dietary pattern score was associated with higher meat and fat intake, and a higher DFA dietary pattern was associated with a higher intake of dairy products. Although the Japanese and DFA dietary patterns were similar in terms of high vegetable and fruit intake, the Japanese dietary pattern differed from the DFA pattern in terms of high intakes of sodium, fish, soybean, seaweeds and green tea.

During 7 years of follow-up (252 647 person-years), we documented 801 deaths from CVD. These deaths included 181 CHDs, 432 total strokes (163 cerebral infarctions, 129 ICHs). Table 4 shows the association between the three dietary pattern score quartiles and CVD mortality. The Japanese dietary pattern was associated with a reduced risk of CVD mortality. On the other hand, the 'animal food' dietary pattern was associated with an increased risk of CVD mortality, and the DFA dietary pattern was not associated with CVD mortality.

After adjustment for age, sex, smoking status, walking duration, education and total energy intake, the multivariate HRs (95% CI) of CVD mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.76 (0.63–0.93), 0.71 (0.58–0.87) and 0.73 (0.59–0.90) ($P$ for trend = 0.003), whereas for the 'animal food' dietary pattern, the corresponding multivariate HRs (95% CI) of CVD mortality were 1.00, 0.93 (0.76–1.13), 1.13 (0.92–1.38) and 1.22 (0.99–1.51) ($P$ for trend = 0.03). With additional adjustment for body mass index and history of hypertension, the results were essentially unchanged. Furthermore, the results of analysis using body mass index as a continuous variable and history of hypertension remained similar.

As the Japanese and 'animal food' dietary patterns were associated with CVD mortality, their associations with CHD and stroke were further investigated (Table 5). After adjusting for potential confounders, the point estimate of the HR for CHD mortality of participants with the highest quartile of the Japanese dietary pattern score was 20% lower than the lowest, whereas those with the highest quartile of the 'animal food' dietary pattern score was 49% higher.

The multivariate HRs (95% CI) of CHD mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.84 (0.56–1.26), 0.70 (0.45–1.08) and 0.80 (0.51–1.25) ($P$ for trend = 0.24), and the corresponding multivariate HRs (95% CI) of the 'animal food' dietary pattern score were 1.00,

**Table 2** Baseline characteristics of the participants according to dietary pattern score quartiles

| | Dietary pattern score quartiles | | | |
|---|---|---|---|---|
| **Characteristic** | 1 (lowest) | 2 | 3 | 4 (highest) |
| **Age (years), mean (SD)** | | | | |
| Japanese pattern | 57.7 (11.1) | 59.3 (10.5) | 60.6 (9.9) | 61.9 (9.3) |
| 'Animal food' pattern | 63.8 (8.9) | 60.6 (10.1) | 58.2 (10.4) | 57.0 (10.6) |
| DFA[a] pattern | 58.5 (10.1) | 60.5 (10.4) | 60.5 (10.4) | 60.1 (10.4) |
| **Male (%)** | | | | |
| Japanese pattern | 55.3 | 48.3 | 43.4 | 41.3 |
| 'Animal food' pattern | 23.5 | 42.2 | 53.4 | 69.1 |
| DFA[a] pattern | 89.8 | 53.0 | 28.8 | 16.7 |
| **Body mass index (kg/m$^2$), mean (SD)** | | | | |
| Japanese pattern | 23.4 (3.3) | 23.5 (3.2) | 23.5 (3.1) | 23.6 (3.1) |
| 'Animal food' pattern | 23.8 (3.4) | 23.6 (3.2) | 23.5 (3.1) | 23.3 (3.0) |
| DFA[a] pattern | 23.5 (3.0) | 23.5 (3.3) | 23.7 (3.3) | 23.5 (3.2) |
| **Current smoker (%)** | | | | |
| Japanese pattern | 44.8 | 35.1 | 28.6 | 24.4 |
| 'Animal food' pattern | 18.1 | 30.0 | 36.1 | 46.9 |
| DFA[a] pattern | 58.0 | 35.7 | 21.3 | 14.8 |
| **Walking duration ⩾1 hour/day (%)** | | | | |
| Japanese pattern | 41.2 | 45.0 | 47.7 | 52.1 |
| 'Animal food' pattern | 43.9 | 44.8 | 47.7 | 49.5 |
| DFA[a] pattern | 54.8 | 47.3 | 44.0 | 40.0 |
| **Current drinker (%)** | | | | |
| Japanese pattern | 55.6 | 51.1 | 46.9 | 43.5 |
| 'Animal food' pattern | 29.6 | 45.9 | 54.6 | 64.8 |
| DFA[a] pattern | 80.0 | 49.6 | 34.4 | 29.8 |
| **Education until age ⩾19 years (%)** | | | | |
| Japanese pattern | 8.3 | 7.7 | 7.6 | 7.8 |
| 'Animal food' pattern | 5.8 | 7.3 | 8.9 | 9.4 |
| DFA[a] pattern | 4.4 | 5.8 | 7.8 | 13.4 |
| **History of hypertension (%)** | | | | |
| Japanese pattern | 22.2 | 23.4 | 25.7 | 27.0 |
| 'Animal food' pattern | 31.6 | 26.2 | 21.7 | 18.9 |
| DFA[a] pattern | 22.3 | 25.0 | 25.7 | 25.4 |

[a] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.
SD, standard deviation.

1.12 (0.73–1.72), 1.38 (0.89–2.15) and 1.49 (0.94–2.34) (*P* for trend = 0.06).

The Japanese dietary pattern was associated with a decreased risk of total stroke, cerebral infarction and ICH mortality. The multivariate HRs (95% CI) of total stroke mortality across increasing quartiles of the Japanese dietary pattern score were 1.00, 0.70 (0.54–0.92), 0.66 (0.50–0.87) and 0.64 (0.47–0.85) (*P* for trend = 0.003). The 'animal food' dietary pattern was not positively associated with the risk of total stroke.

We analysed the association between the Japanese dietary pattern derived from participants who left no blanks for food items ($n = 17\,010$) and CVD mortality, and the results were similar. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.74 (0.51–1.07) (*P* for trend = 0.04). After exclusion of participants who reported daily energy intakes at the extreme 2.5% instead of the extreme 0.5% of the upper or lower ends of the range, we analysed the association between the Japanese dietary pattern derived and CVD mortality ($n = 38\,937$), and the results were similar. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.75 (0.60–0.93) (*P* for trend = 0.005).

After excluding the 287 participants who died from CVD in the first 3 years of follow-up, the multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.70 (0.54–0.92)

**Table 3** Daily nutrient and food intakes of the participants according to dietary pattern score quartiles

| Variable | Dietary pattern score quartiles | | | |
|---|---|---|---|---|
| | 1 (lowest) | 2 | 3 | 4 (highest) |
| **Daily nutrient and food intakes[a] (median)** | | | | |
| **Energy (kJ)** | | | | |
| Japanese pattern | 5046 | 5793 | 6227 | 6861 |
| 'Animal food' pattern | 5128 | 5826 | 6430 | 7458 |
| DFA[b] pattern | 8346 | 5956 | 5537 | 5466 |
| **Fat (g)** | | | | |
| Japanese pattern | 31 | 35 | 38 | 41 |
| 'Animal food' pattern | 34 | 35 | 37 | 41 |
| DFA[b] pattern | 32 | 35 | 37 | 41 |
| **Protein (g)** | | | | |
| Japanese pattern | 61 | 66 | 70 | 74 |
| 'Animal food' pattern | 65 | 66 | 68 | 72 |
| DFA[b] pattern | 68 | 67 | 67 | 69 |
| **Sodium (mg)** | | | | |
| Japanese pattern | 2418 | 2762 | 2925 | 3152 |
| 'Animal food' pattern | 2909 | 2824 | 2768 | 2822 |
| DFA[b] pattern | 2684 | 2865 | 2897 | 2878 |
| **Rice (g)** | | | | |
| Japanese pattern | 814 | 684 | 620 | 567 |
| 'Animal food' pattern | 617 | 647 | 734 | 744 |
| DFA[b] pattern | 885 | 739 | 601 | 524 |
| **Total meats (g)** | | | | |
| Japanese pattern | 20 | 21 | 22 | 22 |
| 'Animal food' pattern | 14 | 19 | 24 | 34 |
| DFA[b] pattern | 21 | 21 | 21 | 22 |
| **Dairy products (g)** | | | | |
| Japanese pattern | 127 | 191 | 217 | 223 |
| 'Animal food' pattern | 192 | 198 | 201 | 206 |
| DFA[b] pattern | 86 | 142 | 226 | 268 |
| **Total Fish (g)** | | | | |
| Japanese pattern | 50 | 64 | 73 | 96 |
| 'Animal food' pattern | 68 | 67 | 66 | 69 |
| DFA[b] pattern | 69 | 67 | 66 | 68 |
| **Total vegetables (g)** | | | | |
| Japanese pattern | 59 | 79 | 99 | 138 |
| 'Animal food' pattern | 101 | 89 | 86 | 87 |
| DFA[b] pattern | 66 | 82 | 96 | 118 |
| **Soybean (g)** | | | | |
| Japanese pattern | 64 | 82 | 98 | 101 |
| 'Animal food' pattern | 95 | 88 | 85 | 87 |
| DFA[b] pattern | 87 | 86 | 89 | 92 |
| **Seaweeds (g)** | | | | |
| Japanese pattern | 3 | 5 | 6 | 9 |
| 'Animal food' pattern | 6 | 5 | 5 | 5 |
| DFA[b] pattern | 4 | 5 | 6 | 7 |
| **Total fruits (g)** | | | | |
| Japanese pattern | 111 | 145 | 173 | 204 |
| 'Animal food' pattern | 178 | 155 | 147 | 147 |
| DFA[b] pattern | 79 | 132 | 183 | 238 |
| **Green tea consumption ⩾5 cups/day (%)** | | | | |
| Japanese pattern | 16 | 26 | 33 | 44 |
| 'Animal food' pattern | 39 | 31 | 26 | 25 |
| DFA[b] pattern | 29 | 30 | 30 | 32 |

[a] Nutrient and food intakes presented in this table are adjusted for total energy intake.
[b] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.

($P$ for trend = 0.009). We performed additional analysis restricted to participants who performed vigorous activity and with a well self-perceived health status ($n$ = 27 239, 312 deaths from CVD), and a similar result was obtained. The multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.71 (0.50–1.01) ($P$ for trend = 0.07). When we used the model adjusted for total energy intake by the residual method, the multivariate HR (95% CI) of CVD mortality for the highest quartile of the Japanese dietary pattern score vs the lowest was 0.78 (0.64–0.96) ($P$ for trend = 0.03).

The results of further analysis stratified by smoking status on the association between the Japanese dietary pattern and CVD mortality are shown in Table 6. Although the point estimates of the HR for CVD mortality were consistently below unity compared with the reference category, the inverse association was less pronounced among current smokers than among never or past smokers ($P$ = 0.07 for interaction with smoking). No interaction between the other covariates and quartiles of the Japanese dietary pattern score was observed (data not shown).

## Discussion

We identified three dietary patterns among the Japanese population: the Japanese, 'animal food' and DFA dietary patterns. The Japanese dietary pattern was associated with a decreased risk of CVD mortality. In contrast, the 'animal food' dietary pattern was associated with an increased risk of CVD mortality, and the DFA dietary pattern was not.

Three dietary patterns we identified were consistent with previously reported patterns observed among different Japanese populations.[20–23] Corresponding to the (i) Japanese, (ii) 'animal food' and (iii) DFA dietary patterns, the previous studies reported dietary patterns that were correlated with (i) vegetables, fruits, seaweeds, soy products and fish,[20–23] (ii) meat and fat[20–23] and (iii) rice (negatively), miso soup (negatively) or bread and dairy products.[20,22,23] Although our FFQ is short, it includes these key foods, especially Japanese foods.

**Table 4** Age, sex-adjusted and multivariate-adjusted hazard ratio for cardiovascular disease mortality according to dietary pattern score quartiles

| Dietary pattern | Dietary pattern score quartiles | | | | P for Trend |
|---|---|---|---|---|---|
| | 1 (low) | 2 | 3 | 4 (high) | |
| **Japanese pattern** | | | | | |
| No. of deaths | 243 | 189 | 179 | 190 | |
| Person-years | 62 529 | 63 035 | 63 316 | 63 767 | |
| Age, sex-adjusted HR (95% CI) | 1 | 0.73 (0.60–0.88) | 0.64 (0.53–0.78) | 0.63 (0.52–0.77) | <0.001 |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.76 (0.63–0.93) | 0.71 (0.58–0.87) | 0.73 (0.59–0.90) | 0.003 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.77 (0.63–0.94) | 0.71 (0.58–0.88) | 0.74 (0.59–0.91) | 0.004 |
| **'Animal food' pattern** | | | | | |
| No. of deaths | 244 | 188 | 184 | 185 | |
| Person-years | 63 113 | 63 396 | 63 143 | 62 996 | |
| Age, sex-adjusted HR (95% CI) | 1 | 0.90 (0.74–1.09) | 1.04 (0.85–1.27) | 1.07 (0.88–1.32) | 0.31 |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.93 (0.76–1.13) | 1.13 (0.92–1.38) | 1.22 (0.99–1.51) | 0.03 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.93 (0.76–1.13) | 1.14 (0.93–1.39) | 1.24 (1.00–1.54) | 0.02 |
| **DFA[c] pattern** | | | | | |
| No. of deaths | 180 | 251 | 211 | 159 | |
| Person-years | 63 303 | 62 878 | 62 848 | 63 618 | |
| Age, sex-adjusted HR (95% CI) | 1 | 1.27 (1.04–1.55) | 1.17 (0.94–1.45) | 0.94 (0.74–1.19) | 0.38 |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 1.18 (0.96–1.45) | 1.07 (0.85–1.35) | 0.88 (0.68–1.13) | 0.14 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 1.18 (0.96–1.45) | 1.10 (0.87–1.38) | 0.89 (0.69–1.14) | 0.19 |

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes/day and currently smoking 20 cigarettes/day), walking duration (<1 hour/day and 1 hour/day), education (until age up to 15 years, until age 16–18 years, and until age 19 years) and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index (<18.5 kg/m$^2$, 18.5–24.9 kg/m$^2$ and 25 kg/m$^2$), and history of hypertension (yes or no).

[c] DFA means high-dairy, high-fruit-and-vegetable, low-alcohol.

HR, hazard ratio; CI, confidence interval.

The Japanese dietary pattern has partly similar characteristics to 'healthy' dietary patterns reported previously among Western populations that were inversely associated with CVD mortality. High consumption of vegetables and fruits is a common component of 'healthy' dietary patterns in Western populations.[13–19] These components might partly explain the possible protective effect of the Japanese dietary pattern against CVD mortality including CHD and stroke, although we might have failed to detect associations with CHD mortality due to insufficient statistical power. However, compared with 'healthy' dietary patterns among Western populations, the Japanese dietary pattern also has unique characteristics.

The Japanese diet has so far been considered to increase the risk of CVD because it includes a large amount of salt.[35] In the present study, the Japanese dietary pattern was related to higher sodium consumption (Table 3) and higher prevalence of hypertension (Table 2). In spite of these risk factors, the Japanese dietary pattern was associated with lower CVD mortality. Although some components of the Japanese diet (i.e. salt) increase the risk of hypertension, other components may compensate for this, and decrease the risk of CVD. Components unique to the Japanese diet would include items such as soybeans, seaweeds and green tea. The effect of those foods upon CVD risk has yet to be clarified.

Factor analysis has both strengths and limitations. On the one hand, it can overcome multicollinearity of various dietary variables, because it is a statistical dimension-reduction technique that exploits the correlation of each variable. However, factor analysis requires several decisions about the methods used for extracting initial factors and rotation.[36] Even after multiple sensitivity analyses using these methods and various groupings by age and sex, the dietary patterns were essentially unchanged.

Our study also had other limitations. First, healthy behaviour in adhering to a Japanese dietary pattern could have confounded the association between dietary patterns and mortality. Although we adjusted our data using measured potential confounders including non-dietary variables, we could not completely exclude the effects of unmeasured confounders. Second, 12% of the participants were lost to follow-up. This proportion did not vary across the quartiles of each dietary pattern score (13%, 13%, 12% and 11% of participants from the lowest to highest Japanese dietary pattern score quartiles, respectively). Therefore, we consider it unlikely that the association between each dietary pattern and CVD mortality was substantially distorted by the effect of loss to follow-up.

Third, our FFQ did not ask about individual portion size, and preparation of foods including added oil. Some misclassification of food consumption could have arisen in deriving dietary pattern scores and estimating the effect of the patterns on

**Table 5** Multivariate-adjusted hazard ratio for coronary heart disease and stroke mortality according to dietary pattern score quartiles

| Variable | Dietary pattern score quartiles | | | | *P* for Trend |
|---|---|---|---|---|---|
| | 1 (low) | 2 | 3 | 4 (high) | |
| **Coronary heart disease** | | | | | |
| **Japanese pattern** | | | | | |
| No. of deaths | 54 | 45 | 38 | 44 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.84 (0.56–1.26) | 0.70 (0.45–1.08) | 0.80 (0.51–1.25) | 0.24 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.86 (0.57–1.29) | 0.71 (0.46–1.11) | 0.82 (0.52–1.29) | 0.29 |
| **'Animal food' pattern** | | | | | |
| No. of deaths | 42 | 44 | 46 | 49 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 1.12 (0.73–1.72) | 1.38 (0.89–2.15) | 1.49 (0.94–2.34) | 0.06 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 1.10 (0.72–1.70) | 1.39 (0.89–2.16) | 1.50 (0.95–2.37) | 0.05 |
| **Total stroke** | | | | | |
| **Japanese pattern** | | | | | |
| No. of deaths | 138 | 100 | 97 | 97 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.70 (0.54–0.92) | 0.66 (0.50–0.87) | 0.64 (0.47–0.85) | 0.003 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.71 (0.54–0.92) | 0.67 (0.51–0.88) | 0.64 (0.48–0.86) | 0.004 |
| **'Animal food' pattern** | | | | | |
| No. of deaths | 142 | 103 | 103 | 84 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.89 (0.68–1.15) | 1.11 (0.84–1.43) | 0.97 (0.72–1.31) | 0.79 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.89 (0.69–1.15) | 1.11 (0.85–1.45) | 1.00 (0.74–1.35) | 0.66 |
| **Cerebral infarction** | | | | | |
| **Japanese pattern** | | | | | |
| No. of deaths | 48 | 44 | 38 | 33 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.89 (0.59–1.36) | 0.73 (0.47–1.15) | 0.60 (0.37–0.99) | 0.03 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.89 (0.59–1.36) | 0.73 (0.47–1.15) | 0.60 (0.37–0.99) | 0.03 |
| **'Animal food' pattern** | | | | | |
| No. of deaths | 51 | 43 | 35 | 34 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 1.04 (0.68–1.57) | 1.08 (0.69–1.70) | 1.11 (0.69–1.78) | 0.66 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 1.03 (0.68–1.56) | 1.09 (0.69–1.71) | 1.14 (0.71–1.85) | 0.57 |
| **Intracerebral hemorrhage** | | | | | |
| **Japanese pattern** | | | | | |
| No. of deaths | 45 | 29 | 25 | 30 | 0.04 |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.62 (0.38–1.00) | 0.52 (0.31–0.87) | 0.60 (0.35–1.01) | 0.04 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.63 (0.39–1.02) | 0.52 (0.31–0.88) | 0.60 (0.36–1.03) | |
| **'Animal food' pattern** | | | | | |
| No. of deaths | 44 | 28 | 30 | 27 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.71 (0.44–1.15) | 0.87 (0.53–1.43) | 0.82 (0.48–1.41) | 0.59 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.71 (0.44–1.16) | 0.89 (0.54–1.46) | 0.86 (0.50–1.47) | 0.71 |

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, smoking status (never, former, currently smoking <20 cigarettes/day and currently smoking 20 cigarettes/day), walking duration (<1 hour/day and 1 hour/day), education (until age up to 15 years, until age 16–18 years, and until age 19 years), and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index (<18.5 kg/m$^2$, 18.5–24.9 kg/m$^2$, and 25 kg/m$^2$) and history of hypertension (yes or no).

HR, hazard ratio; CI, confidence interval.

**Table 6** Multivariate-adjusted hazard ratio for cardiovascular disease mortality according to the Japanese dietary pattern score quartiles stratified by smoking status

| Variable | Dietary pattern score quartiles | | | | *P* for Trend |
|---|---|---|---|---|---|
| | 1 (low) | 2 | 3 | 4 (high) | |
| **Never smoker** | | | | | |
| No. of deaths | 82 | 71 | 76 | 73 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.70 (0.50–0.97) | 0.68 (0.48–0.95) | 0.54 (0.38–0.78) | 0.002 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.70 (0.50–0.97) | 0.68 (0.48–0.95) | 0.54 (0.37–0.78) | 0.002 |
| **Past smoker** | | | | | |
| No. of deaths | 53 | 28 | 30 | 27 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.53 (0.33–0.85) | 0.53 (0.33–0.85) | 0.53 (0.32–0.89) | 0.01 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.53 (0.33–0.85) | 0.53 (0.33–0.86) | 0.53 (0.32–0.89) | 0.01 |
| **Current smoker** | | | | | |
| No. of deaths | 87 | 62 | 45 | 61 | |
| Multivariate-adjusted HR1[a] (95% CI) | 1 | 0.79 (0.57–1.10) | 0.66 (0.46–0.97) | 0.92 (0.64–1.33) | 0.41 |
| Multivariate-adjusted HR2[b] (95% CI) | 1 | 0.79 (0.57–1.11) | 0.66 (0.46–0.97) | 0.93 (0.65–1.34) | 0.44 |

HR, hazard ratio; CI, confidence interval.

[a] Multivariate-adjusted HR1 was adjusted for age (in years), sex, walking duration (<1 hour/day and ≥ 1 hour/day), education (until age up to 15 years, until age 16-18 years, and until age ≥ 19 years), and total energy intake (continuous).

[b] Multivariate-adjusted HR2 was adjusted for the same as HR1, body mass index (<18.5kg/m2, 18.5-24.9kg/m$^2$, and ≥ 25kg/m2), and history of hypertension (yes or no).

CVD mortality. However, this misclassification may be non-differential and would tend to result in underestimation of the impact of the dietary patterns.

In conclusion, we have found that the Japanese dietary pattern is associated with lower CVD mortality, despite the fact that the Japanese dietary pattern appeared to be related to higher sodium intake and high prevalence of hypertension.

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**Conflict of interest**: None declared.

**KEY MESSAGES**

- Although ecological observations suggest that the Japanese diet may reduce the risk of cardiovascular disease, the impact of a Japanese dietary pattern upon mortality due to CVD is unclear.
- The association between dietary patterns among 40 547 Japanese aged 40–79 years and CVD mortality was examined in a 7-year prospective cohort study.
- The Japanese dietary pattern was associated with a lower risk of CVD mortality, despite its relation to sodium intake.

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