Dietary Habits and Risk of Lung Cancer Death in a Large-scale Cohort Study (JACC Study) in Japan by Sex and Smoking Habit

Kotaro Ozasa,1 Yoshiyuki Watanabe,1 Yoshiinori Ito,2 Koji Suzuki,3 Akiko Tamakoshi,3 Nao Seki,4 Yoshikazu Nishino,5 Takaaki Kondo,6 Kenji Wakai,3 Masahiko Ando3 and Yoshiyuki Ohno3 for the JACC Study Group7

1Department of Social Medicine and Cultural Sciences, Research Institute for Neurological Diseases and Geriatrics, Kyoto Prefectural University of Medicine, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto 602-8566, 2Department of Public Health, Fujita Health University School of Health Sciences, 1-98 Dengakugakubo, Kutsukake-cho, Toyoake, Aichi 470-1192, 3Department of Preventive Medicine/Biostatistics and Medical Decision Making, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, 4Division of Public Health, Department of Infectious Disease Control and International Medicine (Course for Community Disease Control), Niigata University Graduate School of Medical and Dental Science, 1-757 Asahimachidori, Niigata 951-8510, 5Division of Epidemiology, Department of Public Health and Forensic Medicine, Tohoku University Graduate School of Medicine, 2-1 Seiryo-machi, Aoba-ku, Sendai 980-8575 and 6Department of Public Health/Health Information Dynamics, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Lung cancer has increased and is the leading cause of cancer death among Japanese males. The associations of dietary habits with the risk of lung cancer death were evaluated by sex and smoking habits in this study. In the Japan Collaborative Cohort (JACC) Study, a cohort established in 1988–90 and consisting of 42 940 males and 55 308 females was observed for lung cancer deaths up to the end of 1997. During the observation period, 446 males and 126 females died of lung cancer. A self-administered food frequency questionnaire was used as the baseline survey. Hazard ratios for dietary factors were calculated by Cox’s proportional hazards model. Among males, a high intake of ham and sausages, cheese, green-leafy vegetables, oranges, and other fruits significantly and dose-dependently decreased the risk of lung cancer death. Among females, a high intake of miso-soup, ham and sausages, and liver significantly and almost dose-dependently increased the risk. Vegetables and fruits rich in antioxidative and carcinogenic agents reduced the risk of lung cancer deaths among male smokers more than among female nonsmokers. The results among female nonsmokers were partially consistent with the hypothesis that high fat consumption increases the risk of lung cancer, especially that of adenocarcinoma.

Key words: Diet — Lung cancer — Cohort study — Epidemiology

The associations between diet and lung cancer have been argued in numerous epidemiologic studies. A high consumption of green-yellow vegetables or fruits has been believed to reduce the risk of lung cancer although some β-carotene intervention studies resulted in failure.1–7 It is considered that experimental mutagenesis and carcinogenesis in animals could be inhibited by a large number of compounds from edible plants, including carotenoids, polyphenols, thiols, trace metals, terpenes, tocopherols, and degradation products of glucosinolates.8 Recently, the protective activity of vegetables and fruits has been focused on antioxidative micronutrients such as carotenoids, vitamin C, folate and others, and recent studies have been focusing on the interactions among them.1–8 Some studies reported that the protective effect of vegetables and fruits was stronger among current smokers than among nonsmokers.9–11 It is thought that antioxidants strongly reduce the oxidative stress due to smoking. However, among nonsmokers, the effect of antioxidants is relatively small because nonsmokers are under less oxidative stress, or their already low risk of lung cancer is not reduced further.9, 10 It has been thought that high fat consumption increases the risk of lung cancer,1, 2 but different effects of animal, plant and fish fats or oils remain to be argued.12, 13

In Japan, Hirayama’s study has been the only large-scale cohort study for evaluating lifestyles and cancer risk; it started in 1965 and was completed around 20 years ago.14 Diet was examined in that study, but the diet of Japanese people has rapidly changed since the Hirayama’s study. Fat consumption increased from 46.5 g per capita in 1965 to 58.3 g in 1988 and consumption of green-yellow vegetables also increased from 49.0 g to 72.8 g per capita. In contrast, consumption of cereals decreased from 418.5 g to 289.2 g per capita during the same period.15 Recent
case-control studies in Japan showed that raw vegetables and fruits reduced the lung cancer risk among smokers and ex-smokers\(^{16}\) and that preserved foods increased, while soyfoods decreased, the risk of lung cancer.\(^{15}\) Thus, a new, and more comprehensive cohort study is necessary to evaluate the dietary risk of cancer. The Japan Collaborative Cohort Study for Evaluation of Cancer Risk sponsored by Monbusho (JACC Study) was planned in the late 1980’s as a new large-scale cohort study surveying people more comprehensively and detailing their lifestyles, while preserving sera of the participants in the baseline survey.\(^{18}\) The new cohort consisted of people in various areas in Japan and was checked for deaths up to the end of 1997. In the present study, we examined the association of lung cancer death with the diet as surveyed by the baseline questionnaire, with special reference to the association by sex and smoking habits.

SUBJECTS AND METHODS

In the JACC Study, a cohort of 46,465 males and 64,327 females aged 40 to 79 years in 45 areas in Japan completed the baseline survey during 1988–1990.\(^{18}\) The areas were selected from 19 prefectures throughout Japan. The cohort consisted of the whole general population (39% of the subjects in this present study), participants in health checkups for a local community (52% of them) and others (voluntary groups, etc.). A self-administered questionnaire for the survey included past and family histories, health conditions and lifestyle habits such as smoking, drinking, diet, physical exercise, occupation, and others. The same questionnaire was used in every area in this study in principle, but some questions differed by area for regional reasons.

For diet, the questionnaire elicited the intake frequency of 32 food items and the number of dishes of boiled rice and miso-soup eaten a day. The subjects were asked about their average diet at the time of the baseline survey. The 32 items were beef, pork, ham and sausages, chicken, liver, egg, milk, yogurt, cheese, butter, margarine, fried foods, fried vegetables, fish (raw, grilled or boiled fish, excluding processed and preserved fish), boiled fish paste (‘kamaboko’ in Japanese), dried or salted fish, green-leafy vegetables, carrots and squash, tomatoes, cabbage and lettuce, Chinese cabbage, edible wild plants (‘sansai’ in Japanese), mushroom, potatoes, seaweed, pickles, foods boiled down in soy sauce (‘tsukudani’ in Japanese), boiled beans, tofu (soybean curd), oranges, fruits other than oranges, and fruit juice. There were five categories of frequency (scarcely any, 1–2 times a month, 1–2 times a week, 3–4 times a week, and almost every day).

Some questions about diet were not asked in some areas for regional reasons. The questions about 16 items (liver, cheese to fried vegetables, boiled fish paste, green-leafy vegetables, Chinese cabbage, mushroom, foods boiled down in soy sauce to fruit juice, in the above list) were put to 83–88% of the subjects and the questions about other items were put to more than 90% of them.

The validity of this food frequency questionnaire was evaluated by comparing it with dietary records for 8 males and 77 females selected from the study areas. Spearman’s correlation coefficients for the frequencies were more than 0.6 for ham and sausages, milk and margarine, and less than 0.2 for liver, fried foods, fried vegetables, boiled fish paste, dried or salted fish, Chinese cabbage, wild edible plants, foods boiled down in soy sauce, and the other foods ranged between them (Date C. et al., unpublished data).

For the present study, the subjects were limited to 42,940 males and 55,308 females who had no history of lung cancer and answered the question about their smoking status. Non-responders to the question about smoking status were 3.2% of the male subjects and 13.4% of the female subjects, probably because nonsmoking women seem to have less concern about the question on smoking. The subjects were checked for death using death certificates by permission of the Management and Coordination Agency of the Japanese Government from their entry into this study up to the end of 1997. All deceased people in the study areas and people who moved out of the study areas were identified using the population registry by permission of each municipality office. During the observation period, 1167 males (2.7%) and 1718 females (3.1%) were censored because they moved out of the study areas. A total 4864 males and 2953 females died, including those who died of lung cancer, during the period. The mean observation period was 92 months (SD; 21 months). Death from lung cancer was defined by the code ‘C34’ in the ICD-10 (International Statistical Classification of Diseases and Related Health Problems, Tenth Revision). The histologic type of lung cancer was rarely given on death certificates, so we analyzed lung cancer as a whole.

The subjects who died of lung cancer during the observation period were 446 males and 126 females. Table I shows the number of subjects and lung cancer cases by smoking status. The hazard ratios (HRs) for dietary risk factors were separately estimated among males and females, and then among smoking-status groups by sex (male current smokers, male ex-smokers and female non-smokers). The other smoking-status groups were not analyzed because of insufficient numbers of lung cancer cases. The ratios were adjusted for age (numeric), father’s or mother’s history of lung cancer (dichotomous), and in addition, smoking index (levels of <20, 20–39, 40–59, 60–79, 80–99 and 100+ pack-years) among current smokers, and the period after quitting smoking (levels of <5, 5–9, 10–14, 15–19 and 20+ years) among ex-smokers. All these factors were considered in calculating HRs.
among males and females, respectively. Passive smoking at home was evaluated dichotomously in the questionnaire. The effect was not significant among female nonsmokers (HR = 0.80, 95% CI: 0.49, 1.28). Consequently, it was not used in computing the adjusted HRs among them. The ratios were not adjusted for total energy or its surrogates because the subjects’ diet was measured by a simple food frequency method for limited food items.

The five categories of food frequency, and quantity of boiled rice and miso-soup were integrated into three groups by considering the number of subjects in each group and a meaningful cut-off frequency. HRs of the highest and intermediate intake compared with the lowest were calculated with Cox’s proportional hazards model using the PHREG procedure in the SAS package. The HRs were obtained by stratification of 19 prefectures using the ‘strata’ statement of the procedure, because diet may differ by area. The dose-response trend was tested by evaluating the regression coefficient when the three intake categories were treated as equally-spaced numeric variables in the Cox model. \( P \) values less than 0.05 were considered significant. This investigation was approved by the Ethical Board of Nagoya University School of Medicine.

RESULTS

HRs of lung cancer deaths associated with diet are presented in Tables II to V, which show the items significant at the level of \( P < 0.1 \) for at least one category (fish for males and females, oranges for male ex-smokers, and green-leafy vegetables and oranges for female nonsmokers are exceptions because the items are noteworthy). Among all males (Table II), a high intake of ham and sausages, cheese, green-leafy vegetables, oranges, and other fruits significantly and dose-dependently decreased the risk of lung cancer death. The HRs of the highest intakes compared with the lowest were 0.72 (95% CI: 0.52, 0.99) for ham and sausages, 0.59 (0.38, 0.91) for cheese, 0.76 (0.59, 0.98) for green-leafy vegetables, 0.75 (0.57, 0.99) for oranges, and 0.73 (0.55, 0.97) for other fruits. In addition, yogurt, butter, carrots and squash, tomatoes, boiled beans, and fruit juice, had significantly low HRs (range 0.70–0.74) for intermediate intake compared with the lowest. Among all females (Table II), a high intake of miso-soup, ham and sausages, and liver significantly and almost dose-dependently increased the risk (HR = 1.92 (95% CI: 1.00, 3.67), 1.79 (1.07, 3.01), and 2.25 (1.02, 4.94) for the highest intake, respectively). Tofu had a significantly low HR (0.50) for the intermediate intake without dose-dependency.

Among male current smokers (Table III), a high intake of boiled rice in their 30s significantly and dose-dependently increased the risk of lung cancer death (HR = 1.93, 95% CI: 1.11, 3.36, for the highest intake). A high intake of oranges and other fruits significantly and almost dose-dependently decreased the risk (HR = 0.66 (95% CI: 0.47, 0.91), and 0.71 (0.50, 0.99) for the highest intake, respectively). Milk, yogurt, cheese, butter and carrots and squash, tomatoes, and fruit juice had significantly low HRs (range 0.64–0.70) for intermediate intake compared with the lowest.

Among male ex-smokers (Table IV), cheese consumption had an inverse association with lung cancer death (HR = 0.24, 95% CI: 0.07, 0.81) for the highest intake vs. the lowest. Foods boiled down with soy sauce had a significantly high HR (1.76) for intermediate intake.

Intake of other foods, not shown in Tables II to V, was not associated with lung cancer death among each group. In addition, excluding lung cancer deaths within two years after the baseline survey did not substantially alter the results.

DISCUSSION

The risk of lung cancer was evaluated for each sex and separately for groups classified by sex and smoking status in our study. The reason was, first, that the characteristics of lung cancer were associated with smoking status of the subjects. The proportions of squamous cell carcinoma, small cell carcinoma and adenocarcinoma cases ranged from 34.3 to 38.5%, from 12.6 to 15.5%, and from 29.2 to 41.4%, respectively, among males in the four cancer registries of Japan in 1987–1992. Among females, the corresponding proportions ranged from 8.5 to 13.8%, from 6.4 to 11.7%, and from 55.4 to 69.5%. This sex difference in distribution of histologic type is thought to reflect the difference in smoking rates by sex in Japan (60.5% for males...
Table II. Hazard Ratios (HRs) of Lung Cancer Death for Diet and 95% Confidence Intervals (CIs) Adjusted by Age, Parents’ History of Lung Cancer, Smoking Status, Smoking Index, and Time since Quitting Smoking

| Item                  | Category          | Person-years | Deaths | HR  | 95%CI    | P       | Person-years | Deaths | HR  | 95%CI    | P       |
|-----------------------|-------------------|--------------|--------|-----|----------|---------|--------------|--------|-----|----------|---------|
| Boiled rice in the 30s| 0–2 dishes/day    | 90 085       | 101    | 1.00|          |         |              |        |     |          |         |
|                       | 3–5 dishes/day    | 108 679      | 120    | 1.48| 0.96–2.29| 0.072   |              |        |     |          |         |
|                       | 6+ dishes/day     | 136 273      | 214    | 1.43| 0.94–2.18| 0.092   |              |        |     |          |         |
| Boiled rice in the 30s| trend P=0.54      |              |        |     |          |         |              |        |     |          |         |
| Miso-soup             | <1 dish/day       | 113 683      | 146    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2 dishes/day    | 134 802      | 173    | 1.06| 0.82–1.36| 0.63    |              |        |     |          |         |
|                       | 3+ dishes/day     | 73 032       | 102    | 1.14| 0.83–1.57| 0.38    |              |        |     |          |         |
| Miso-soup             | trend P=0.69      |              |        |     |          |         |              |        |     |          |         |
| Ham & sausages        | ≤1–2/m            | 137 613      | 192    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/w             | 108 510      | 116    | 0.90| 0.71–1.52| 0.42    |              |        |     |          |         |
|                       | 3–4/w+            | 56 234       | 54     | 0.72| 0.52–0.99| 0.044   |              |        |     |          |         |
| Ham & sausages        | trend P=0.049     |              |        |     |          |         |              |        |     |          |         |
| Liver                 | ≤1–2/m            | 187 313      | 212    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/w             | 32 033       | 35     | 0.82| 0.55–1.22| 0.33    |              |        |     |          |         |
|                       | 3–4/w+            | 33 901       | 40     | 0.78| 0.47–1.29| 0.34    |              |        |     |          |         |
| Liver                 | trend P=0.049     |              |        |     |          |         |              |        |     |          |         |
| Milk                  | Scarcely any      | 57 481       | 91     | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/m to 3–4/w    | 141 154      | 146    | 0.76| 0.58–1.01| 0.066   |              |        |     |          |         |
|                       | trend P=0.48      |              |        |     |          |         |              |        |     |          |         |
| Milk                  | trend P=0.051     |              |        |     |          |         |              |        |     |          |         |
| Yogurt                | Scarcely any      | 164 351      | 203    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/m to 1–2/w    | 68 002       | 56     | 0.71| 0.52–0.98| 0.039   |              |        |     |          |         |
|                       | 3–4/w+            | 43 607       | 49     | 0.81| 0.54–1.22| 0.32    |              |        |     |          |         |
| Yogurt                | trend P=0.14      |              |        |     |          |         |              |        |     |          |         |
| Yogurt                | trend P=0.39      |              |        |     |          |         |              |        |     |          |         |
| Cheese                | Scarcely any      | 128 092      | 180    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/m to 1–2/w    | 124 424      | 112    | 0.71| 0.55–0.92| 0.0092  |              |        |     |          |         |
|                       | 3–4/w+            | 30 246       | 28     | 0.59| 0.38–0.91| 0.017   |              |        |     |          |         |
| Cheese                | trend P=0.0029    |              |        |     |          |         |              |        |     |          |         |
| Cheese                | trend P=0.33      |              |        |     |          |         |              |        |     |          |         |
| Butter                | Scarcely any      | 126 736      | 165    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/m to 1–2/w    | 111 309      | 95     | 0.71| 0.54–0.92| 0.011   |              |        |     |          |         |
|                       | 3–4/w+            | 42 272       | 57     | 0.92| 0.65–1.30| 0.66    |              |        |     |          |         |
| Butter                | trend P=0.23      |              |        |     |          |         |              |        |     |          |         |
| Butter                | trend P=0.023     |              |        |     |          |         |              |        |     |          |         |
| Margarine             | Scarcely any      | 101 451      | 135    | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/m to 1–2/w    | 111 543      | 103    | 0.77| 0.57–1.02| 0.073   |              |        |     |          |         |
|                       | 3–4/w+            | 41 909       | 53     | 0.92| 0.65–1.28| 0.63    |              |        |     |          |         |
| Margarine             | trend P=0.41      |              |        |     |          |         |              |        |     |          |         |
| Margarine             | trend P=0.41      |              |        |     |          |         |              |        |     |          |         |
| Fried foods           | ≤1–2/m            | 73 052       | 86     | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/w             | 129 688      | 150    | 0.99| 0.76–1.29| 0.95    |              |        |     |          |         |
|                       | 3–4/w+            | 74 575       | 97     | 1.12| 0.82–1.51| 0.45    |              |        |     |          |         |
| Fried foods           | trend P=0.45      |              |        |     |          |         |              |        |     |          |         |
| Fried foods           | trend P=0.19      |              |        |     |          |         |              |        |     |          |         |
| Fried vegetables      | ≤1–2/m            | 62 731       | 80     | 1.00|          |         |              |        |     |          |         |
|                       | 1–2/w             | 126 008      | 126    | 0.78| 0.59–1.04| 0.095   |              |        |     |          |         |
|                       | 3–4/w+            | 93 108       | 136    | 1.02| 0.77–1.36| 0.84    |              |        |     |          |         |
| Fried vegetables      | trend P=0.57      |              |        |     |          |         |              |        |     |          |         |
| Fried vegetables      | trend P=0.56      |              |        |     |          |         |              |        |     |          |         |
| Fish                  | ≤1–2/w            | 150 457      | 184    | 1.00|          |         |              |        |     |          |         |
|                       | 3–4/w             | 85 300       | 112    | 1.12| 0.87–1.43| 0.36    |              |        |     |          |         |
|                       | Almost every day  | 69 552       | 91     | 1.03| 0.79–1.34| 0.81    |              |        |     |          |         |
| Fish                  | trend P=0.72      |              |        |     |          |         |              |        |     |          |         |
| Fish                  | trend P=0.50      |              |        |     |          |         |              |        |     |          |         |

1262
Table II. (Continued)

| Item                  | Category | Person-years | Deaths | HR   | 95% CI      | P       | Person-years | Deaths | HR   | 95% CI      | P       |
|-----------------------|----------|--------------|--------|------|-------------|---------|--------------|--------|------|-------------|---------|
| Fish paste (Kamaboko) | ≤1–2/m   | 161 534      | 201    | 1.00 |             |         | 200 482      | 52     | 1.00 |             |         |
|                       | 1–2/w    | 78 613       | 83     | 0.84 | 0.64–1.09   | 0.19    | 108 330      | 30     | 1.12 | 0.71–1.78   | 0.60    |
|                       | 3–4/w+   | 36 766       | 38     | 0.73 | 0.51–1.05   | 0.093   | 49 121       | 19     | 1.58 | 0.91–2.73   | 0.099   |
| Green-leafy vegetables| ≤1–2/w   | 124 585      | 164    | 1.00 |             |         | 141 206      | 32     | 1.00 |             |         |
|                       | 3–4/w    | 93 429       | 118    | 0.90 | 0.71–1.14   | 0.40    | 126 177      | 35     | 1.18 | 0.73–1.91   | 0.48    |
|                       | Almost every day | 91 722 | 106 | 0.76 | 0.59–0.98 | 0.034 | 133 889 | 41 | 1.19 | 0.75–1.90 | 0.44 |
| Carrots & squash      | ≤1–2/m   | 66 639       | 96     | 1.00 |             |         | 47 760       | 11     | 1.00 |             |         |
|                       | 1–2/w    | 106 671      | 114    | 0.71 | 0.54–0.94   | 0.017   | 131 903      | 36     | 1.33 | 0.67–2.62   | 0.41    |
|                       | 3–4/w+   | 104 878      | 137    | 0.84 | 0.64–1.10   | 0.22    | 198 034      | 52     | 1.24 | 0.64–2.41   | 0.51    |
| Tomatoes              | ≤1–2/m   | 124 840      | 163    | 1.00 |             |         | 131 978      | 36     | 1.00 |             |         |
|                       | 1–2/w    | 90 808       | 85     | 0.70 | 0.54–0.92   | 0.010   | 117 262      | 22     | 0.75 | 0.44–1.28   | 0.30    |
|                       | 3–4/w+   | 81 190       | 92     | 0.90 | 0.70–1.16   | 0.43    | 142 617      | 47     | 1.21 | 0.76–1.94   | 0.40    |
| Seaweed               | ≤1–2/w   | 140 174      | 188    | 1.00 |             |         | 143 102      | 43     | 1.00 |             |         |
|                       | 3–4/w    | 89 630       | 105    | 0.86 | 0.68–1.10   | 0.24    | 123 558      | 31     | 0.88 | 0.55–1.41   | 0.62    |
|                       | Almost every day | 79 760 | 93 | 0.78 | 0.60–1.00 | 0.24 | 141 291 | 34 | 0.77 | 0.49–1.23 | 0.28 |
| Boiled beans          | ≤1–2/m   | 153 868      | 187    | 1.00 |             |         | 191 543      | 47     | 1.00 |             |         |
|                       | 1–2/w    | 64 811       | 66     | 0.74 | 0.56–0.99   | 0.043   | 89 205       | 23     | 0.96 | 0.58–1.60   | 0.89    |
|                       | 3–4/w+   | 44 528       | 62     | 0.90 | 0.67–1.21   | 0.51    | 73 650       | 17     | 0.81 | 0.46–1.44   | 0.47    |
| Tofu (soybean curd)   | ≤1–2/m   | 108 467      | 149    | 1.00 |             |         | 121 809      | 41     | 1.00 |             |         |
|                       | 3–4/w    | 84 667       | 94     | 0.80 | 0.62–1.04   | 0.10    | 115 861      | 18     | 0.50 | 0.28–0.88   | 0.016   |
|                       | Almost every day | 72 837 | 93 | 0.83 | 0.63–1.08 | 0.17 | 120 932 | 32 | 0.85 | 0.52–1.37 | 0.51 |
| Oranges               | ≤1–2/m   | 59 999       | 87     | 1.00 |             |         | 46 440       | 12     | 1.00 |             |         |
|                       | 1–2/w    | 68 496       | 86     | 0.88 | 0.65–1.19   | 0.41    | 73 087       | 16     | 0.92 | 0.43–1.97   | 0.84    |
|                       | 3–4/w+   | 131 490      | 148    | 0.75 | 0.57–0.99   | 0.045   | 236 107      | 64     | 1.10 | 0.58–2.09   | 0.76    |
| Fruits other than oranges | ≤1–2/m | 47 428 | 81 | 1.00 |         |         | 36 480 | 13 | 1.00 |         |         |
|                       | 1–2/w    | 70 508       | 78     | 0.71 | 0.52–0.98   | 0.038   | 67 655       | 15     | 0.71 | 0.33–1.51   | 0.38    |
|                       | 3–4/w+   | 130 690      | 141    | 0.73 | 0.55–0.97   | 0.029   | 234 644      | 56     | 0.80 | 0.42–1.50   | 0.49    |
| Fruit juice           | ≤1–2/m   | 97 243       | 139    | 1.00 |             |         | 133 242      | 33     | 1.00 |             |         |
|                       | 1–2/w    | 61 087       | 53     | 0.70 | 0.51–0.96   | 0.030   | 72 692       | 18     | 1.16 | 0.65–2.07   | 0.60    |
|                       | 3–4/w+   | 77 128       | 91     | 0.90 | 0.69–1.18   | 0.45    | 112 644      | 24     | 0.95 | 0.56–1.63   | 0.87    |

Abbreviations: 1–2/m=once or twice a month, 1–2/w=once or twice a week, 3–4/w=3–4 times a week.

1) Smoking index=quantity of cigarettes smoked per day × duration of smoking (year), for current smokers.

and 14.3% for females in 1990)\textsuperscript{21} and that in association of smoking and lung cancer by histologic type.\textsuperscript{22} Squamous cell carcinoma, small cell carcinoma and adenocarcinoma accounted for 42.6%, 15.9% and 34.4% of lung cancer in male current smokers, respectively. The corresponding proportions were 51.8%, 14.6% and 30.7% for male ex-smokers and 10.3%, 6.3% and 78.9% for female nonsmokers (recalculated from Sobue’s data\textsuperscript{23}). Therefore, a high proportion of squamous cell and small cell carcinoma compared with adenocarcinoma for male current and ex-smokers could be assumed in our cohort, with the opposite distribution for female nonsmokers.
Second, diet is thought to interact with smoking. Smoking is the strongest lifestyle risk factor for lung cancer. Tobacco and tobacco smoke contain many tumorigenic agents such as polynuclear aromatic hydrocarbons, N-nitrosamines, aromatic amines, and other organic and inorganic compounds. In addition, free radicals and single oxygen derived from cigarette smoke produce carcinogenic oxidative stress. Fruits and vegetables are

| Item                  | Category          | Person-years | Deaths | HR      | 95%CI     | P     |
|-----------------------|-------------------|--------------|--------|---------|-----------|-------|
| Boiled rice in the 30s| 0–2 dishes/day    | 47 402       | 56     | 1.00    |           |       |
|                       | 3–5 dishes/day    | 59 232       | 81     | 1.82    | 1.03–3.21 | 0.038 |
|                       | 6+ dishes/day     | 69 762       | 159    | 1.93    | 1.11–3.36 | 0.018 |
|                       | trend P=0.043     |              |        |         |           |       |
| Ham & sausages        | ≤1–2/m            | 73 539       | 143    | 1.00    |           |       |
|                       | 1–2/w             | 56 590       | 71     | 0.77    | 0.58–1.04 | 0.090 |
|                       | 3–4/w+            | 29 309       | 36     | 0.68    | 0.46–1.00 | 0.050 |
|                       | trend P=0.026     |              |        |         |           |       |
|                       | 1–2/m to 3–4/w    | 77 419       | 95     | 0.70    | 0.50–0.97 | 0.036 |
|                       | Almost every day  | 55 272       | 96     | 0.86    | 0.63–1.18 | 0.36  |
| Milk                  | Scarcely any      | 34 247       | 72     | 1.00    |           |       |
|                       | 1–2/m to 3–4/w    | 77 419       | 95     | 0.70    | 0.50–0.97 | 0.036 |
|                       | Almost every day  | 55 272       | 96     | 0.86    | 0.63–1.18 | 0.36  |
| Yogurt                | Scarcely any      | 90 449       | 145    | 1.00    |           |       |
|                       | 1–2/m to 3–4/w    | 32 869       | 33     | 0.64    | 0.42–0.97 | 0.035 |
|                       | 3–4/w+            | 21 494       | 28     | 0.69    | 0.41–1.18 | 0.18  |
|                       | trend P=0.069     |              |        |         |           |       |
| Cheese                | Scarcely any      | 68 627       | 124    | 1.00    |           |       |
|                       | 1–2/m to 3–4/w    | 63 815       | 68     | 0.67    | 0.49–0.92 | 0.015 |
|                       | 3–4/w+            | 16 203       | 23     | 0.76    | 0.46–1.25 | 0.28  |
|                       | trend P=0.057     |              |        |         |           |       |
| Butter                | Scarcely any      | 65 680       | 113    | 1.00    |           |       |
|                       | 1–2/m to 3–4/w    | 58 811       | 61     | 0.65    | 0.47–0.90 | 0.011 |
|                       | 3–4/w+            | 23 006       | 40     | 0.94    | 0.62–1.42 | 0.77  |
|                       | trend P=0.29      |              |        |         |           |       |
| Green-leafy vegetables| ≤1–2/w            | 69 399       | 111    | 1.00    |           |       |
|                       | 3–4/w             | 48 247       | 82     | 0.98    | 0.73–1.30 | 0.91  |
|                       | Almost every day  | 44 960       | 70     | 0.80    | 0.59–1.09 | 0.17  |
|                       | trend P=0.18      |              |        |         |           |       |
| Carrots & squash      | ≤1–2/m            | 69 192       | 69     | 1.00    |           |       |
|                       | 1–2/w             | 47 099       | 76     | 0.69    | 0.49–0.96 | 0.030 |
|                       | 3–4/w+            | 39 849       | 92     | 0.86    | 0.62–1.19 | 0.38  |
|                       | trend P=0.51      |              |        |         |           |       |
| Tomatoes              | ≤1–2/m            | 36 038       | 116    | 1.00    |           |       |
|                       | 1–2/w             | 36 463       | 57     | 0.68    | 0.49–0.94 | 0.019 |
|                       | 3–4/w+            | 64 203       | 78     | 0.91    | 0.67–1.23 | 0.54  |
|                       | trend P=0.42      |              |        |         |           |       |
| Oranges               | ≤1–2/m            | 28 707       | 69     | 1.00    |           |       |
|                       | 1–2/w             | 38 929       | 58     | 0.78    | 0.55–1.11 | 0.17  |
|                       | 3–4/w+            | 63 294       | 94     | 0.66    | 0.47–0.91 | 0.012 |
|                       | trend P=0.013     |              |        |         |           |       |
| Fruits other than oranges| ≤1–2/m         | 52 021       | 61     | 1.00    |           |       |
|                       | 1–2/w             | 31 869       | 56     | 0.70    | 0.49–1.02 | 0.065 |
|                       | 3–4/w+            | 40 105       | 90     | 0.71    | 0.50–0.99 | 0.044 |
|                       | trend P=0.062     |              |        |         |           |       |
| Fruit juice           | ≤1–2/m            | 51 846       | 96     | 1.00    |           |       |
|                       | 1–2/w             | 31 773       | 34     | 0.66    | 0.44–0.98 | 0.040 |
|                       | 3–4/w+            | 40 003       | 62     | 0.91    | 0.66–1.26 | 0.58  |
|                       | trend P=0.46      |              |        |         |           |       |

Abbreviations: 1–2/m=once or twice a month, 1–2/w=once or twice a week, 3–4/w=3–4 times a week.
HRs were adjusted by age, parents’ history of lung cancer and smoking index.
rich in antioxidant micronutrients such as carotenoids as well as other anti-carcinogenic agents. Therefore, protection is thought to work more effectively among smokers than among nonsmokers. Diet is confounded with smoking. Foods that were regarded as good for health were more frequently eaten by nonsmokers than smokers. For example, the subjects who drank milk almost every day were 34% of current smokers, 43% of ex-smokers, and 44% of nonsmokers among male subjects in this study, and they were 31%, 42%, and 44%, respectively, among females. The subjects eating oranges 3–4 times a week or more frequently were 47% of current smokers, 55% of ex-smokers, and 52% of nonsmokers among males, and they were 56%, 62%, and 67% among females. Other dairy foods, fruits, and green-yellow vegetables showed similar findings. The difference in intake of those foods within each smoking status was smaller than the difference by smoking status (see above). The subjects who drank milk almost every day were from 33% to 37% at various smoking index levels among male current smokers. Those eating oranges 3–4 times a week or more frequently were from 45% to 50%. Other dairy foods, fruits, and green-yellow vegetables also showed similar findings, and those proportions were less dose-dependent on smoking index. Therefore, residual confounding by smoking on these foods was thought to be small.

This cohort consisted of the respondents to the questionnaire survey from the whole general population and participants in health checkups. This means that this cohort may be more health-conscious and have better lifestyles than the general population itself. This bias could make it difficult to detect the protective effect of good lifestyles. In this cohort, health-conscious people tended to eat more dairy products and green-yellow vegetables. For example, the subjects who drank milk almost every day were 46% of those taking a great interest in health checkup (answer to another question in this cohort questionnaire) among the male subjects in this current study, compared with 36% of those taking no interest. Among the female subjects, the corresponding values were 53% and 36%. Those eating green-leafy vegetables almost every day were 33% and 27%, among males, and 40% and 33% among females, respectively. Other dairy foods and green-yellow vegetables showed similar findings.

The protective effect of higher intake of fruits and vegetables for lung cancer is widely accepted, despite the negative results in β-carotene intervention studies. The

---

### Table IV. Hazard Ratios (HRs) of Lung Cancer Death for Diet and 95% Confidence Intervals (CIs) among Male Ex-smokers

| Item Category | Person-years | Deaths | HR  | 95% CI       | P     |
|---------------|--------------|--------|-----|-------------|-------|
| Boiled rice at present | 0–2 dishes/day | 21 867 | 36  | 1.00 |       |
|                | 3–5 dishes/day | 53 522 | 65  | 0.80 | 0.52–1.22 | 0.30 |
|                | 6+ dishes/day | 11 544 | 7   | 0.45 | 0.19–1.06 | 0.069 |
| Cheese        | Scarcely any | 32 069 | 45  | 1.00 |       |
|                | 1–2/m to 1–2/w | 33 859 | 31  | 0.69 | 0.42–1.15 | 0.16 |
|                | 3–4/w+ | 7 392  | 3   | 0.24 | 0.07–0.81 | 0.022 |
| Green-leafy vegetables | ≤1–2/w | 30 394 | 40  | 1.00 |       |
|                | 3–4/w | 25 199 | 30  | 0.82 | 0.51–1.33 | 0.43 |
|                | Almost every day | 25 549 | 26  | 0.65 | 0.39–1.07 | 0.091 |
| Foods boiled down with soy sauce (tsukudani) | ≤1–2/m | 36 084 | 31  | 1.00 |       |
|                | 1–2/w | 19 372 | 29  | 1.76 | 1.05–2.93 | 0.030 |
|                | 3–4/w+ | 14 121 | 14  | 1.07 | 0.56–2.04 | 0.81 |
| Oranges       | ≤1–2/m | 12 916 | 13  | 1.00 |       |
|                | 1–2/w | 17 136 | 22  | 1.39 | 0.70–2.79 | 0.34 |
|                | 3–4/w+ | 36 998 | 42  | 1.22 | 0.64–2.33 | 0.53 |

Abbreviations: 1–2/m=once or twice a month, 1–2/w=once or twice a week, 3–4/w=3–4 times a week.

HRs were adjusted by age, parents’ history of lung cancer and time since quitting smoking.
discrepancy between the observation studies and intervention could be explained by the possibility that the excessive doses of \(\beta\)-carotene given in those intervention studies may be carcinogenic in vivo, and that the cooperative action of carotenoids and other compounds in fruits and vegetables is necessary to inhibit carcinogenesis.\(^1\),\(^3\)–\(^7\)

Recently, flavonoids in vegetables, which scavenge free radicals and are strongly antioxidative, have been added to the list of protective compounds.\(^24\),\(^25\)

A high intake of green-leafy vegetables, oranges and other fruits was, in our study, associated with a significant dose-dependent reduction in risk of lung cancer among males, and a high intake of the latter two was also associated among male current smokers. This result was consistent with numerous previous studies.\(^1\)–\(^7\),\(^14\) However, significantly low HRs were not observed for the highest intake of carrots and squash, and tomatoes. Exposure misclassification may be larger among males than females because males do not usually cook themselves and cannot exactly evaluate their intake of those vegetables. In contrast, fruit consumption could be reported better, because fruits are eaten by choice. It was reported that the correlation between a food frequency questionnaire and four 4-day dietary records was better in females than in males for green-yellow vegetables and almost equal between the sexes for fruits.\(^26\) The comparison by sex was difficult in our validity data because most of the subjects were females.

Consumption of green-yellow vegetables has increased in Japan\(^15\) and it may have reached a sufficient level to protect against carcinogenesis among most people. This cohort may be health-conscious and have consumed large amounts of green-yellow vegetables. In addition, people at a high health risk may increase their intake of green-yellow vegetables, because they have been promoted as being good for health. Those may be additional reasons why green-yellow vegetables did not show a clear protective effect.

Table V. Hazard Ratios (HRs) of Lung Cancer Death for Diet and 95% Confidence Intervals (CIs) among Female Nonsmokers

| Item                  | Person-years | Deaths | HR   | 95% CI        | P     |
|-----------------------|--------------|--------|------|---------------|-------|
| Miso-soup             |              |        |      |               |       |
| <1 dish/day           | 147 825      | 30     | 1.00 | 0.89–2.56     | 0.12  |
| 1–2 dishes/day        | 186 192      | 48     | 1.51 | 0.85–3.71     | 0.12  |
| 3+ dishes/day         | 55 440       | 16     | 1.77 | 0.65–4.65     | 0.12  |
| trend P=0.059         |              |        |      |               |       |
| Ham & sausages        |              |        |      |               |       |
| ≤1–2/m                | 171 838      | 34     | 1.00 | 0.73–2.06     | 0.12  |
| 1–2/w                 | 132 680      | 28     | 1.23 | 0.73–2.06     | 0.12  |
| 3–4/w+                | 65 768       | 24     | 2.02 | 1.15–3.53     | 0.12  |
| trend P=0.059         |              |        |      |               |       |
| Liver                 |              |        |      |               |       |
| ≤1–2/m                | 243 103      | 43     | 1.00 | 0.66–3.02     | 0.12  |
| 1–2/w                 | 33 626       | 9      | 1.43 | 0.66–3.02     | 0.12  |
| 3–4/w+                | 36 529       | 15     | 2.29 | 0.95–5.47     | 0.12  |
| trend P=0.061         |              |        |      |               |       |
| Fried foods           |              |        |      |               |       |
| ≤1–2/m                | 96 003       | 15     | 1.00 | 0.79–2.70     | 0.12  |
| 1–2/w                 | 165 130      | 35     | 1.47 | 0.79–2.70     | 0.12  |
| 3–4/w+                | 83 589       | 24     | 2.29 | 0.95–5.47     | 0.12  |
| trend P=0.056         |              |        |      |               |       |
| Green-leafy vegetables|              |        |      |               |       |
| ≤1–2/w                | 130 087      | 23     | 1.00 | 0.68–2.09     | 0.12  |
| 3–4/w                 | 118 378      | 27     | 1.19 | 0.68–2.09     | 0.12  |
| Almost every day       | 126 081      | 35     | 1.35 | 0.79–2.30     | 0.12  |
| trend P=0.061         |              |        |      |               |       |
| Tofu (soybean curd)   |              |        |      |               |       |
| ≤1–2/w                | 112 025      | 30     | 1.00 | 0.48–0.86     | 0.12  |
| 3–4/w                 | 109 028      | 13     | 0.45 | 0.48–0.86     | 0.12  |
| Almost every day       | 115 137      | 29     | 0.90 | 0.53–1.53     | 0.12  |
| trend P=0.070         |              |        |      |               |       |
| Oranges               |              |        |      |               |       |
| ≤1–2/m                | 42 090       | 8      | 1.00 | 0.35–2.34     | 0.12  |
| 1–2/w                 | 68 271       | 12     | 0.95 | 0.35–2.34     | 0.12  |
| 3–4/w+                | 223 275      | 53     | 1.18 | 0.54–2.57     | 0.12  |
| trend P=0.053         |              |        |      |               |       |

Abbreviations: 1–2/m=once or twice a month, 1–2/w=once or twice a week, 3–4/w=3–4 times a week. HRs were adjusted by age and parents’ history of lung cancer.
Among females (also female nonsmokers), fruits and green-yellow vegetables were not associated with any reduction in risk of lung cancer. These results seemed to be inconsistent with the theory that high fruit or vegetable consumption reduces the risk of lung cancer. The exposure misclassification would tend to be smaller for females because they usually cook for themselves, so that it does not seem to have caused these obscure results. Intake of these foods did not seem to be strongly related to other diet risks. The possible reason is that the protection afforded by antioxidants and other protective agents may work less among nonsmokers because they have low oxidative stress and a smaller intake of carcinogenic agents. Some other studies showed similar results to our study.3–11)

Among male ex-smokers, vegetables and fruits showed weaker protective effects than among current smokers. The reason may be that ex-smokers had less oxidative stress and smaller amounts of carcinogens derived from smoking because they quit smoking.

A high intake of cheese was associated with a reduction in the risk of lung cancer among all males and male ex-smokers. Some studies reported a risk reduction due to cheese and attributed it to the high vitamin A content.27, 28) However, it has recently been thought that the protective effect of total dietary vitamin A may reflect the effect of carotenoids, rather than retinol itself.23) Dairy foods are recognized as healthy in Japan, and the subjects interested in health checkup had a high intake of dairy foods in this study, so that high consumption of dairy foods may be related to underlying healthy lifestyle factors which reduce lung cancer risk in general.

It has been reported that high consumption of saturated fat and red meat increased the risk of lung cancer in analytical epidemiologic studies.3, 7) Most studies showed a stronger association among men than women,11 but a study group showed an increased risk of lung cancer for a high total and saturated fat intake and red meat consumption among nonsmoking women, with a stronger association for adenocarcinoma.4, 12, 29) Our study showed an increased risk of lung cancer for a high intake of ham and sausages, and liver, and no decreased risks for a high intake of dairy foods were observed among females, despite the decreased risk among males. These results are partially consistent with the theories put forward in previous studies.

Associations of intake of ham and sausages, and liver with lung cancer deaths by sex were unclear. When the HRs for ham and sausages were additionally adjusted for cheese, green-leafy vegetables, and fruits other than oranges, the point estimate of HR for the highest intake compared with the lowest was still low among males (0.68, \(P=0.14\)). This hardly seems to suggest that the low HR was due to confounding by intake of dairy foods, vegetables, and fruits. Therefore, the result is still not explicable. On the other hand, the high HRs for a high intake of ham and sausages, and liver among females were thought to reflect the association of fat-rich foods and adenocarcinoma. The association between dairy foods and potential healthy lifestyles may be cancelled from the viewpoint of fat intake, because dairy foods are rich in saturated fat and seem to be related to a Western-style diet, which is also richer in saturated fat than a Japanese-style diet.

A high intake of boiled rice in the 30s was positively associated with lung cancer death among male current smokers. Much consumption of boiled rice in the age of manhood may be associated with physical labor. This implies low socioeconomic status, which may be a potential risk factor. A high intake of miso-soup was also positively associated among females. Consumption of miso-soup seems to be associated with Japanese-style diet and increased salt intake. However, the significance of these findings is unclear.

In conclusion, in this large-scale cohort study in Japan, frequent vegetable and fruit consumption significantly decreased the risk of lung cancer death among males. This suggests that antioxidative micronutrients and anticarcinogenic agents rich in vegetables and fruits reduced oxidative stress and carcinogenesis due to smoking. Frequent intake of ham and sausages, and liver increased the risk among females, which is partially consistent with the hypothesis that high saturated fat consumption increases the risk of lung cancer, especially that of adenocarcinoma. Frequent intake of cheese may decrease the risk among males, but its consumption may reflect other concomitant healthy lifestyle factors.

ACKNOWLEDGMENTS

The authors wish to express their appreciation to Dr. Kunio Aoki, Professor Emeritus, Nagoya University School of Medicine and the former chairman of the JACC Study Group, and Dr. Haruo Sugano, the former Director, Cancer Institute of Japanese Foundation for Cancer Research, who greatly contributed to the initiation of the study. The present investigators in the JACC Study Group are as follows: Dr. Y. Ohno, Nagoya University Graduate School of Medicine, Dr. M. Mori, Sapporo Medical University School of Medicine, Dr. Y. Motohashi, Akita University School of Medicine, Dr. S. Hisamichi, Tohoku University Graduate School of Medicine, Dr. Y. Nakamura, Jichi Medical School, Dr. H. Iso, University of Tsukuba, Dr. H. Mikami, Chiba Cancer Center, Dr. S. Hashimoto, University of Tokyo, Dr. Y. Inaba, Juntendo University School of Medicine, Dr. Y. Hoshiyama, Showa University School of Medicine, Dr. H. Suzuki, Niigata University School of Medicine, Dr. H. Shimizu, Gifu University School of Medicine, Dr. H. Toyoshima and Dr. A. Tamakoshi, Nagoya University Graduate School of Medicine, Dr. S. Tokudome, Nagoya City University Medical School, Dr. Y. Ito, Fujita Health University School of Health Sciences, Dr. A. Koizumi, Kyoto University Graduate School of Medicine, Dr. T. Kawamura, Kyoto University Center for Student Health, Dr. Y.
Watanabe and Dr. M. Nakao, Kyoto Prefectural University of Medicine, Dr. C. Date, Osaka City University Medical School, Dr. T. Suzuki, Research Institute Osaka Medical Center for Cancer and Cardiovascular Diseases, Dr. T. Hashimoto, Wakayama Medical University, Dr. T. Nose, Tottori University Faculty of Medicine, Dr. N. Hayakawa, Hiroshima University, Dr. T. Yoshimura, University of Occupational and Environmental Health, Dr. K. Fukuda, Kurume University School of Medicine, Dr. N. Okamoto, Kanagawa Cancer Center, Dr. T. Ishibashi, Asama General Hospital, Dr. H. Shio, Shiga Medical Center, Dr. T. Kitagawa, Cancer Institute of Japanese Foundation for Cancer Research, Dr. T. Kuroki, Gifu University, and Dr. K. Tajima, Aichi Cancer Center Research Institute. The former investigators in the JACC Study Group are presented in reference 18, except for the following two members (affiliations are those when they participated in the study): Dr. T. Shimamoto, University of Tsukuba; and Dr. H. Tanaka, Tokyo Medical and Dental University. This work was supported by a Grant-in-Aid for Scientific Research on Priority Areas (C) (2) (No.12218216) from the Ministry of Education, Science, Sports and Culture of Japan. The JACC Study was also supported by Grants-in-Aid for Scientific Research from the same ministry (No. 63010074, 1010068, 2151065, 3151064, 4151063, 5151069, 6279102 and 11181101).

(Received July 5, 2001/Revised September 22, 2001/Accepted September 26, 2001)

REFERENCES

1) Ziegler, R. G., Taler Mayne, S. and Swanson, C. A. Nutrition and lung cancer. Cancer Causes Control, 7, 157–177 (1996).

2) World Cancer Research Fund/American Institute for Cancer Research. “Food, Nutrition and the Prevention of Cancer: a Global Perspective,” pp. 140–142, 384–398, 405–416 (1997). American Institute for Cancer Research, Washington, DC.

3) Koo, L. C. Diet and lung cancer 20+ years later: more questions than answers? Int. J. Cancer, 50, 22–29 (1997).

4) Brownson, R. C., Alavanja, M. C., Capraro, N., Simes, E. J. and Chang, J. C. Epidemiology and prevention of lung cancer in nonsmokers. Epidemiol. Rev., 20, 218–236 (1998).

5) Du, Y. X., Zhou, B. S. and Wu, J. M. Lifestyle factors and human lung cancer: an overview of recent advances (review). Int. J. Oncol., 13, 471–477 (1998).

6) Biesalski, H. K., de Mesquita, B. B., Chesson, A., Chytir, F., Grimble, R., Hermus, R. J., Kohrer, J., Lotan, R., Norpoth, K., Pastorino, U. and Thurham, D. European consensus statement on lung cancer: risk factors and prevention. Lung Cancer Panel. CA Cancer J. Clin., 48, 167–176 (1998).

7) Cooper, D. A., Eldridge, A. L. and Peters, J. C. Dietary carotenoids and lung cancer: a review of recent research. Natr. Rev., 57, 133–145 (1999).

8) Cross, E. C., Traber, M., Eisierich, J. and van der Vilet, A. Micronutrient antioxidants and smoking. Br. Med. Bull., 55, 691–704 (1999).

9) Voorrips, L. E., Goldbohm, R. A., Brants, H. A., van Poppel, G. A., Sturmans, F., Hermus, R. J. and van den Brandt, P. A. A prospective cohort study on antioxidant and folate intake and male lung cancer risk. Cancer Epidemiol. Biomarkers Prev., 9, 357–365 (2000).

10) Voorrips, L. E., Goldbohm, R. A., Verhoeven, D. T., van Poppel, G. A., Sturmans, F., Hermus, R. J. and van den Brandt, P. A. Vegetable and fruit consumption and lung cancer risk in the Netherlands Cohort Study on diet and cancer. Cancer Causes Control, 11, 101–110 (2000).

11) Yong, L. C., Brown, C. C., Schatzkin, A., Dresser, C. M., Slesinski, M. J., Cox, C. S. and Taylor, P. R. Intake of vitamins E, C, and A and risk of lung cancer. The NHANES I epidemiologic followup study. First National Health and Nutrition Examination Survey. Am. J. Epidemiol., 146, 231–243 (1997).

12) Alavanja, M. C. R., Brown, C. C., Swanson, C. and Brownson, R. C. Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. J. Natl. Cancer Inst., 85, 1906–1916 (1993).

13) Veierod, M. B., Laake, P. and Thelle, D. S. Dietary fat intake and risk of lung cancer: a prospective study of 51,452 Norwegian men and women. Eur. J. Cancer Prev., 6, 540–549 (1997).

14) Hirayama, T. “Life-Style and Mortality. Contributions to Epidemiology and Biostatistics Vol. 6,” pp. 1–27, 73–96 (1990). Karger, Basel.

15) Research Committee of Health and Nutrition Information. “National Nutrition Survey, Japan, 1998,” pp. 145–151 (2000). Daichi-shuppan Co., Tokyo (in Japanese).

16) Gao, C., Tajima, K., Kuroishi, T., Hirose, K. and Inoue, M. Protective effects of raw vegetables and fruit against lung cancer among smokers and ex-smokers: a case-control study in the Tokai Area of Japan. Jpn. J. Cancer Res., 84, 594–600 (1993).

17) Wakai, K., Ohno, Y., Genka, K., Ohmine, K., Kawamura, T., Tamakoshi, A., Lin, Y., Nakayama, T., Aoki, K. and Fukuma, S. Risk modification in lung cancer by a dietary intake of preserved foods and soyfoods: findings from a case-control study in Okinawa, Japan. Lung Cancer, 25, 147–159 (1999).

18) Ohno, Y., Tamakoshi, A. and JACC Study Group. Japan Collaborative Cohort Study for Evaluation of Cancer Risk sponsored by Monbusho (JACC Study). J. Epidemiol., 11, 144–150 (2001).

19) SAS Institute. “SAS Technical Report P-217, SAS/STAT Software: The PHREG Procedure,” pp. 1–52 (1991). SAS Institute Inc., Cary, NC.

20) Parkin, D. M., Whelan, S. L., Ferlay, J., Raymond, L. and Young, J. “Cancer Incidence in Five Continents, VII,” pp. 1076–1079 (1997). IARC, Lyon.
21) Ministry of Health and Welfare, Japan. “Smoking and Health,” 2nd Ed., pp. 270–271 (1993). Hoken-Dojinsha Co., Tokyo (in Japanese).
22) Sobue, T., Suzuki, T., Horai, T., Matsuda, M. and Fujimoto, I. Relationship between cigarette smoking and histologic type of lung cancer, with special reference to sex difference. Jpn. J. Clin. Oncol., 18, 3–13 (1988).
23) U.S. Department of Health and Human Services. “Reducing the Health Consequences of Smoking, 25 Years of Progress,” DHHS Publication No. (CDC) 89-8411, pp. 79–116 (1989). U.S. Department of Health and Human Services, Rockville.
24) Knekt, P., Jarvinen, R., Seppanen, R., Hellovaara, M., Teppo, L., Pukkala, E. and Aromaa, A. Dietary flavonoids and the risk of lung cancer and other malignant neoplasms. Am. J. Epidemiol., 146, 223–230 (1997).
25) Le Marchand, L., Murphy, S. P., Hankin, J. H., Wilkens, L. R. and Kolonel, L. N. Intake of flavonoids and lung cancer. J. Natl. Cancer Inst., 19, 154–160 (2000).
26) Wakai, K., Egami, I., Kato, K., Lin, Y., Kawamura, T., Aoki, R., Kojima, M., Nakayama, T., Wada, M. and Ohno, Y. A simple food frequency questionnaire for Japanese Diet—Part 1. Development of the questionnaire, and reproducibility and validity for food groups. J. Epidemiol., 9, 216–226 (1999).
27) Mayne, S. T., Janerich, D. T., Greenwald, P., Chorost, S., Tucci, C., Zaman, M. B., Melamed, M. R., Kieley, M. and Mckneally, M. F. Dietary beta carotene and lung cancer risk in U.S. nonsmokers. J. Natl. Cancer Inst., 86, 33–38 (1994).
28) Brennan, P., Fortes, C., Butler, J., Agudo, A., Benhamou, S., Darby, S., Gerken, M., Jokel, K. H., Kreuzer, M., Mallone, S., Nyberg, F., Pohlabeln, H., Ferro, G. and Boffeta, P. A multicenter case-control study of diet and lung cancer among non-smokers. Cancer Causes Control, 11, 49–58 (2000).
29) Swanson, C. A., Brown, C. C., Sinha, R., Kulldorff, M., Brownson, R. C. and Alavanja, M. C. Dietary fats and lung cancer risk among women: the Missouri Women’s Health Study (United States). Cancer Causes Control, 8, 883–893 (1997).