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Review

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Dietary Factors, Dietary Patterns, and Cardiovascular Disease Risk in Representative Japanese Cohorts: NIPPON DATA80/90

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Diet is one of the most important factors affecting healthy life expectancy through the onset of cardiovascular disease (CVD) risk as well as various chronic diseases. Because dietary habits and disease structure differ depending on the country, region, and/or race, evidence from each population is required. NIPPON DATA80/90 is a long-term cohort study of a representative Japanese population that participated in national nutrition surveys. Among the many findings of this cohort study, a dietary pattern with higher intake of fruits, vegetables, fish (n-3 polyunsaturated fatty acids), and dietary fiber and lower intake of salt as well as sodium-to-potassium ratio was found to be associated with a lower risk of CVD mortality. The results from our cohort study would be useful for effectively preventing CVD. This article reviews the published studies from the NIPPON DATA80/90 to highlight the significant findings that may be used to develop risk prevention strategies for CVD.

Key words: **Dietary factors, Dietary pattern, Cardiovascular disease risk**

Introduction

Diet is one of most important factors affecting healthy life expectancy through its association with the onset of cardiovascular diseases (CVD) as well as various lifestyle-related chronic diseases. Because dietary habits and disease structure differ depending on the country, region, and/or race, evidence from each population is required. While the relationship between dietary intake and pattern and CVD risk has been investigated and reported, most previous studies were from Western countries, with reports from Asian countries, including Japan, only recently beginning to accumulate. NIPPON DATA is a cohort study of a representative Japanese population that participated in national nutrition surveys. In this review, we describe the findings on dietary factors and patterns as well as CVD mortality risk that have been revealed by the NIPPON DATA80/90 research. The findings from the NIPPON DATA are summarized in **Table 1**.

1. NIPPON DATA80/90

The National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged (NIPPON DATA) is a series of cohort studies principally based on the National Cardiovascular Survey of Japan (NCSJ) and the National Nutrition Survey of Japan (NNSJ). The baseline cohorts of NIPPON DATA80 and NIPPON DATA90 were participants of the 3rd and 4th NCSJ and NNSJ conducted in 1980 and 1990, respectively[1-3]. The participants were residents of 300 survey districts throughout Japan randomly selected for the National Surveys by the Ministry of Health, Labour and Welfare of Japan. Accordingly, the participants in NIPPON DATA are considered representatives of the general Japanese population. In NNSJ, information on dietary intake was collected through weighed dietary records for 3 consecutive days, and the absolute amount of dietary intake, including foods

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Table 1. Summary of published findings from NIPPON DATA studies

Ref.	Dietary factor	Cohort	Duration of Follow-up	Mortality risk			
				Total CVD	CHD	Stroke	All-cause
	Food groups						
13	Fruit	ND80	24 years	↓	ns	↓	–
80	Fruit	ND80	29 years	↓	–	–	–
13	Vegetable	ND80	24 years	↓	↓	ns	–
80	Vegetable	ND80	29 years	↓	–	–	–
13	Fruit and vegetable	ND80	24 years	↓	ns	↓	–
19	Fish	ND80	19 years	–	ns	ns	ns
80	Fish	ND80	29 years	↓	–	–	–
28	Milk and dairy products	ND80	24 years	↓ (for women)	↓	ns	–
33	Egg	ND80	14 years	–	ns	ns	↓ (for women)
34	Egg	ND90	15 years	ns	–	–	↓ (for women)
40	Tofu	ND80	24 years	–	–	↓ (CH for women)	–
	Nutrients						
46	n-3 PUFA	ND80	24 years	↓	ns	ns	–
54	Dietary fiber	ND80	24 years	↓ (for men)	–	↓ (for women)	–
59	Salt	ND80	24 years	↑	↑	↑	↑
80	Salt	ND80	29 years	↑	–	–	–
64	Sodium-to-potassium ratio	ND80	24 years	↑	–	↑	↑
68	Vegetable protein	ND90	15 years	↓	ns	↓ (CH)	–
76	Total energy	ND80	29 years	ns	↑	ns	↑ (for men)

↑, significant positive association; ↓, significant inverse association; ns, not significant; CH, cerebral hemorrhage; CHD, coronary heart disease; CVD, cardiovascular disease; ND, NIPPON DATA; PUFA, polyunsaturated fatty acids.

and macro/micronutrients, was calculated[4, 5]. Meanwhile, follow-up surveys have been conducted every 5 years since 1994 for the NIPPON DATA80 and since 1995 for the NIPPON DATA90, and the vital status and cause of death (including CVD) have been updated[6].

2. Association of Food Consumption with Cardiovascular Risk

2.1. Fruits and Vegetables

Many cohort studies, primarily from Western countries, have confirmed the beneficial effects of fruit and vegetable intake on coronary heart disease (CHD), stroke, and CVD mortality[7-12]. However, studies on the association of fruit and vegetable intake with CVD risk in Asian populations are limited. Therefore, we evaluated the association of fruit and vegetable intake adjusted for energy intake (g/1,000 kcal) with CVD mortality risk using 24-year follow-up data from NIPPON DATA80 [13]. The multivariable-adjusted hazard ratio (HR) for the highest versus the lowest quartile of total fruit and vegetable intake was 0.74 (95% confidence interval [CI]: 0.61–0.91, *P* for trend=0.003) for total CVD, 0.80 (95% CI: 0.59–1.09, *P* for trend=0.036) for stroke, and 0.57 (95% CI: 0.37–0.87, *P* for trend=0.109) for CHD. Similar inverse associations with CVD risk were observed when the analyses were repeated using fruit intake alone and vegetable intake alone **(Fig. 1)**.

In Japan, vegetable intake is often associated with high intake of salt because some people typically use table soy sauce on salted vegetables, and vegetables are often cooked with soy sauce. Several previous studies have demonstrated that the intake of vegetables is not associated with CVD risk[14, 15]. These studies have mostly used food-frequency questionnaires (FFQ) to assess dietary intake. However, it is difficult to accurately evaluate the amount of salt intake using FFQ. Therefore, the lack of adjustment for salt intake could lead to underestimation of the inverse relationship between vegetable intake and CVD risk. In NIPPON DATA80 described above, we used data from 3-day weighed dietary records, from which we could obtain the absolute intake quantities of food, salt, and total energy[13]. Our findings from NIPPON DATA80 indicate that higher intake of vegetable and fruit accompanied by lower intake of salt is important

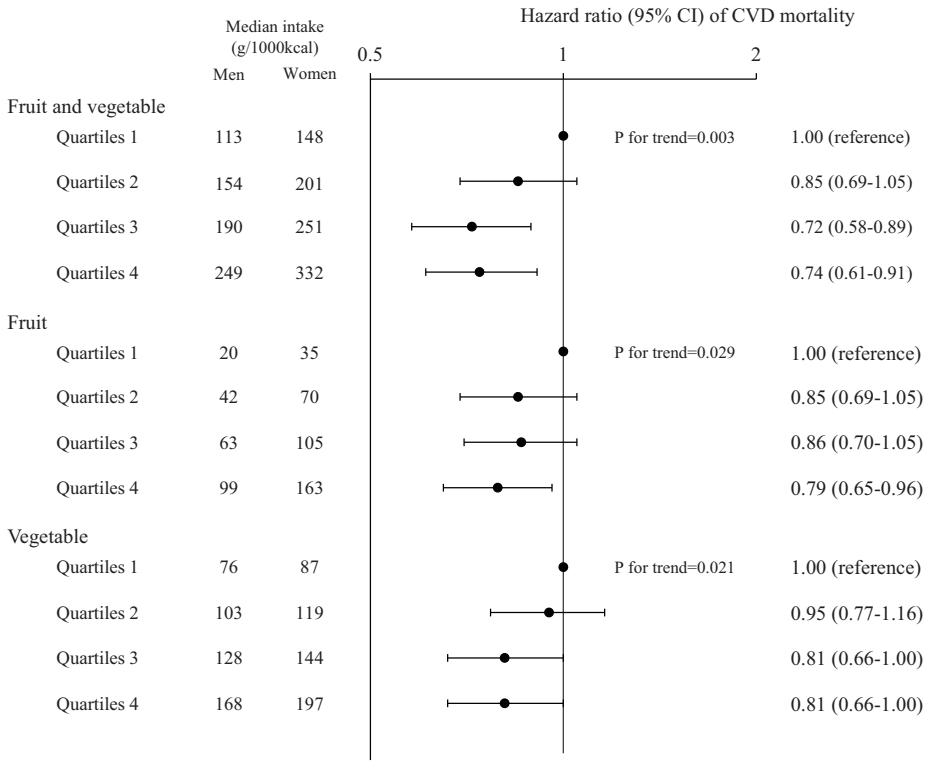

Fig. 1. HRs for CVD mortality according to quartiles of fruit and vegetable intake[13]

HRs were adjusted for age, sex, body mass index (kg/m^2), smoking status (current-, ex-, never), alcohol drinking (daily drinkers and others), sodium intake (mg/1000 kcal), and intakes of meat (g/1000 kcal), fish and shellfish (g/1000 kcal), milk and dairy products (g/1000 kcal), and soybeans and legumes (g/1000 kcal).

to prevent CVD.

2.2. Fish

Many epidemiological studies have evaluated the association of fish intake and CVD risk[16]. The intake of fish in Japan is much higher than that in other countries, including Western countries[17, 18]. Our research group evaluated the association between fish intake and all-cause and cause-specific mortality risk using 19-year follow-up data from NIPPON DATA80[19]. In this study, fish intake was evaluated using the food-frequency method, and the study participants were divided into five groups according to their fish intake frequency. The relative risks of mortality in participants who ate fish more than twice daily compared with those who ate 1–2 times weekly were 0.99 (95% CI: 0.77–1.27) for all-cause mortality, 1.26 (95% CI: 0.70–2.29) for stroke, and 0.91 (95% CI: 0.35–2.35) for CHD. Because detailed data on nutrient and/or other food group intake were not available at that time in our study, these results could not be adjusted for other dietary factors, such as total energy, salt, or meat intake.

2.3. Milk and Dairy Products

Although intake of milk and dairy products is recommended in Japan to ensure nutritional balance, especially adequate amount of calcium and potassium[20, 21], the current dairy intake among the Japanese is much lower than the recommended level[22]. Several cohort studies have suggested that intake of dairy products is inversely associated with CVD risk mainly in the Western population, whose intake is much higher compared with the Japanese population[23-27]. Kondo *et al.* analyzed and reported the association between the intake of milk and dairy products and CVD mortality risk using 24-year follow-up data from NIPPON DATA80[28]. The risk of CVD mortality of the lowest tertile of milk and dairy intake (mean intake: 22.7 g/day) compared with that of the highest (mean intake: 168.3 g/day) was higher in women (HR: 1.27, 95% CI: 0.99–1.58, *P* for trend=0.045); no such relationship was observed in men. In addition to the recommended intake of milk and dairy products to increase calcium and potassium intake, the nutritional role of milk and dairy products should be further evaluated in Japan.

2.4. Egg

Because egg yolk contains relatively high cholesterol, limiting egg intake was often recommended to reduce serum cholesterol concentrations and to prevent CHD[29]. The egg intake in Japan (around five eggs per week) is two times higher than that in the United States (two to three eggs per week), significantly contributing to the total number of cholesterol intake[30-32]. Our research group examined the relationship of egg intake with serum total cholesterol concentration and total and cause-specific mortality risk in the NIPPON DATA80 cohort[33]. In women, a dose–response relationship was observed between the frequency of egg intake evaluated using the FFQ (≥ 2/d, 1/d, 1/2d, 1–2/wk, and seldom) and age-adjusted total cholesterol concentration (5.11, 4.98, 4.89, 4.83, and 4.84 mmol/L, $P<0.0001$). The multivariable-adjusted relative risk of total mortality in the 1–2 eggs/wk group was significantly lower than that in the 1 egg/day group in women (relative risk: 0.78, 95% CI: 0.63–0.96), whereas no such associations were observed in men. There were no clear associations between egg intake and the mortality risk for stroke and ischemic heart disease.

In addition, similar evaluations were conducted using 15-year follow-up data from NIPPON DATA90[34]. The participants were 4,686 women aged ≥ 30 years with no history of stroke or myocardial infarction at baseline. Egg intake was not found to be associated with age-adjusted total cholesterol concentration ($P=0.886$). After adjustment for covariates, the HRs for cancer and total mortality in the ≥ 2 eggs/day group were significantly higher than those in the 1 egg/day group. Egg intake was not found to be related to the risk of CVD mortality.

The association between egg intake and serum cholesterol concentration was inconsistent in our two cohort studies, probably related to the differences in the baseline year, which was 1980 for the NIPPON DATA80 and 1990 for the NIPPON DATA90. In Japan, public awareness of cholesterol concentration as an important risk factor for atherosclerosis was not high until the early 1980s. After the Health and Medical Service Law for the elderly began in 1983, people had the opportunity to learn their cholesterol level through annual health check-ups, and hypercholesterolemic individuals were provided with health services, such as health guidance or education for preventing CHD, particularly the middle-aged and elderly people[35]. Along with these changes, eggs became a popular media symbol for cholesterol, both dietary and blood[36]. Thus, the loss of the association of egg intake with serum cholesterol concentration in NIPPON DATA90 may be due to the avoidance of egg intake among the participants, especially individuals with hypercholesterolemia. Meanwhile, egg intake has been directly associated with cancer and total mortality risk, suggesting that limiting egg intake may have some health benefits, at least in women in Japan[33, 34].

2.5. Tofu (Soy Products)

Soybeans and soy products are traditional foods in many Asian countries, including Japan. Many investigations suggested their health benefits, such as cholesterol-lowering effects[37, 38] and improvement of endothelial function[39]. However, the association of soy products with the risk of CVD, particularly stroke, has not yet been confirmed. Therefore, we evaluated the effects of dietary soy intake on the risk of stroke mortality using 24-year follow-up data from NIPPON DATA80 [40]. Of the soy foods, we focused on tofu as it is the most common form of soy consumed in Japan. The study participants were 9,244 men and women; their mean (standard deviation [SD]) daily tofu intake was 18.6 (18.5) g/1,000 kcal for women and 17.0 (16.2) g/1,000 kcal for men. No significant associations between tofu intake and total mortality or cerebral infarction mortality were observed in either sex. The risk of death from cerebral hemorrhage in the highest quartile of tofu intake was lower than that in the lowest quartile (HR: 0.35, 95% CI: 0.14–0.85, P for trend=0.03) only in women. Stratified analyses by age revealed that the inverse association of tofu intake with cerebral hemorrhage mortality in women was limited to those younger than 65 years. Therefore, the study's finding of a significant association only in younger women may be due simply to chance. Further studies are warranted to confirm the effects of soy foods on stroke risk.

3. Association of Nutrients with Cardiovascular Risk

3.1. Marine-Derived N-3 Polyunsaturated Fatty Acids (PUFA)

The intake of marine-derived n-3 PUFA among the Japanese population is generally higher than that in the Western population[18, 41]. Several cohort studies in Japan have reported an association between marine-derived n-3 PUFA intake and CVD risk; however, the dietary intake in these studies was assessed using the FFQ[42, 43]. Therefore, the results were not controlled for salt intake, which in Japan is generally associated with fish intake[44]. Using 24-year follow-up data from NIPPON DATA80, we investigated the association between marine-derived n-3 PUFA intake and the risk

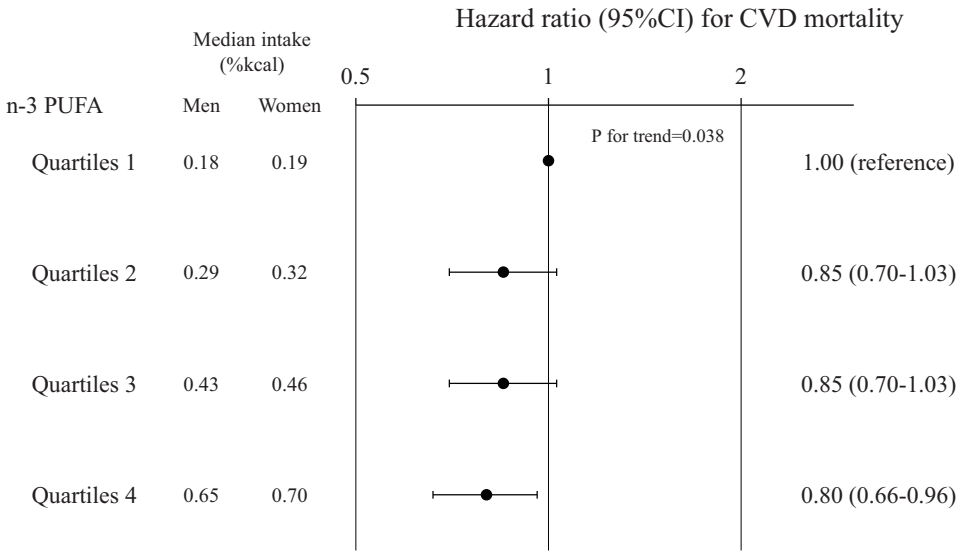

Fig. 2. HRs of CVD mortality by sex-specific quartiles of n-3 PUFA intake[45)]

HRs were adjusted for age, sex, body mass index, smoking status, alcohol drinking, systolic blood pressure, blood glucose, serum total cholesterol, antihypertensive medication status, residential area, and dietary intake of saturated fatty acids, n-6 PUFA, vegetable protein, total dietary fiber, and sodium.

of CVD mortality with adjustment for dietary intake, including salt[45)]. The study participants were 9,190 men and women without a history of CVD at baseline; their median intake of marine-derived n-3 PUFA was 0.37%kcal (0.86 g/day). The risk of CVD mortality in the highest quintile of marine-derived n-3 PUFA was lower than that in the lowest quintile (HR: 0.80, 95% CI: 0.66–0.96), and its inverse linear trend was statistically significant (*P* for trend=0.038) **(Fig. 2)**. The median value of the lowest quintile of marine-derived n-3 PUFA intake (0.18%kcal, 0.4 g/day) was twice as high as the mean intake reported in the US population[46)]. Our findings indicated that a higher intake of marine-derived n-3 PUFA was associated with reduced risk of CVD compared with a modest n-3 PUFA intake.

3.2. Carbohydrates and Dietary Fiber

Carbohydrates are a primary source of energy in the human diet, comprising dietary fiber and available carbohydrate, including starch and sugar. Dietary fiber has several beneficial effects on atherosclerosis, such as reduction of postprandial blood glucose levels[47)], cholesterol levels[48, 49)], and blood pressure[50)]. Furthermore, dietary fiber has been reported to be inversely related with the risk of CHD [48, 51)], stroke[52)], and CVD[48, 51)]. However, few studies have investigated the relationships of each carbohydrate component with CVD mortality risk in the Japanese population. We therefore evaluated the association of the intake of dietary fiber, carbohydrate, available carbohydrate, and starch with the risk of CVD mortality using 24-year follow-up data from NIPPON DATA80 [53)]. The study participants were 8,925 men and women aged 30–79 years without a history of CVD at baseline. After adjustment for covariates, the risk for CVD mortality in men was lower in the highest quintile of dietary fiber intake (HR: 0.64, 95% CI: 0.47–0.87, *P* for trend=0.007) than that in the lowest quintile. A similar but nonsignificant trend toward an association was observed in women (*P* for trend=0.196). Compared with that in the lowest quintile of dietary fiber intake, the risk of stroke mortality was significantly lower in the highest quintile of dietary fiber intake in women (HR: 0.61, 95% CI: 0.38–0.98, *P* for trend=0.046), whereas this association was marginally significant in men (*P* for trend=0.098). However, the intake of carbohydrate, available carbohydrate, or starch was not associated with the risk of CVD mortality in both sexes. These findings indicate that higher intake of dietary fiber should be promoted to prevent CVD. Dietary fiber is divided into two types: insoluble fiber and soluble fiber. Previous studies suggested that dietary fiber may be differentially associated with health outcomes depending on their solubility. However, data of soluble and insoluble fiber were not available in NIPPON DATA80; thus, we could not evaluate the relationships between each type of dietary fiber and CVD risk.

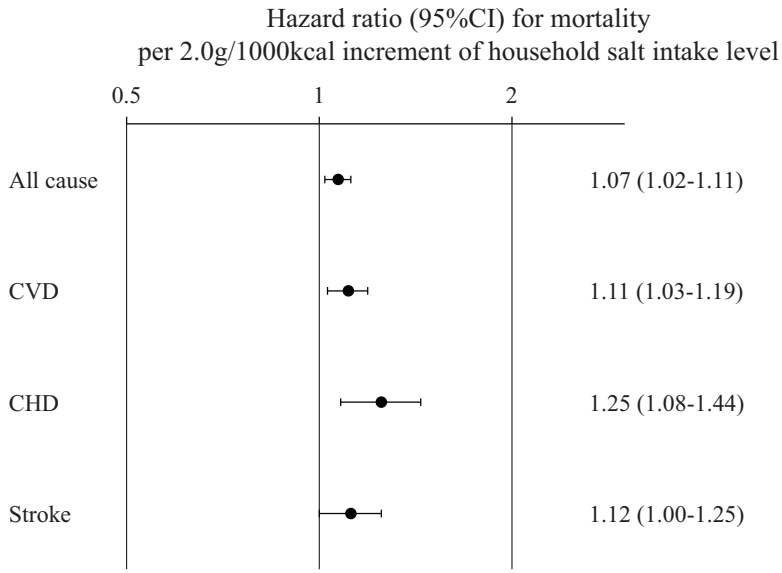

Fig. 3. HRs for mortality per 2.0 g/1000 kcal increment of household salt intake[58]

HRs were adjusted for age, sex, body mass index, smoking status, alcohol drinking, work exertion level, household-based potassium, saturated fatty acids, and long-chain n-3 PUFAs.

3.3. Salt and Sodium-to-Potassium Ratio

Previous cohort studies and meta-analyses have demonstrated that individual salt intake is positively associated with total and cause-specific mortality risk[54-57]. However, few studies have reported the adverse effect of salt intake evaluated at the household level. In NNSJ, dietary intake, including salt, was evaluated by household using the dietary weighing method. We therefore examined the relationship between household salt intake and long-term all-cause mortality, CVD, CHD, and stroke using 24-year follow-up data of NIPPON DATA80 based on the NNSJ[58]. From the analyses of 8,702 men and women, excluding those living alone, the average (SD) household salt intake assessed by simple density in each household was 6.25 (2.02) g/1,000 kcal. A 1-SD (2.0 g/1,000 kcal) higher household salt intake was associated with a higher risk of all-cause mortality (HR: 1.07, 95% CI: 1.02–1.11), CVD (HR: 1.11, 95% CI: 1.03–1.19), CHD (HR: 1.25, 95% CI: 1.08–1.44), and stroke (HR: 1.12, 95% CI: 1.00–1.25) **(Fig. 3)**. In Asian countries, including Japan, the main source of salt is seasoning used in cooking at home, including salt, soy sauce, or miso paste[44, 59, 60]. Hot pot dishes (miso soup or simmered dishes, mostly seasoned with soy sauce) are usually cooked at home and eaten by members in the same household. Our findings from NIPPON DATA80 indicate that targeting interventions at the entire household may be important to the reduction of salt intake population-wide.

Sodium and potassium fluctuate antagonistically: an increase in sodium intake leads to raised blood pressure, whereas an increase in potassium intake leads to reduced blood pressure by increasing sodium excretion. Therefore, the sodium-to-potassium ratio might be a better predictor of future CVD risk than either sodium or potassium intake alone. Although the average intake of sodium among the Japanese population has been decreasing, it still remains high in the worldwide scale. Moreover, the average intake of potassium among the Japanese population remains lower than that among the Western population, and thus, the dietary sodium-to-potassium ratio remains high[61, 62]. Analyses using 24-year follow-up data from NIPPON DATA80 revealed that the mortality risk in the highest quintile of dietary sodium-to-potassium ratio (average: 2.72), compared with that in the lowest quintile (average: 1.25), was significantly higher for all-cause mortality (HR: 1.16, 95% CI: 1.06–1.27), total CVD (HR: 1.39, 95% CI: 1.20–1.61), and stroke (HR: 1.43, 95% CI: 1.17–1.76) **(Fig. 4)**[63]. Reducing sodium (salt) intake as well as increasing potassium intake from fruit and vegetables could be important to address CVD mortality risk in Japan.

3.4. Vegetable Protein

Dietary protein, one of the important nutrients, is classified into animal protein (meat, fish, dairy products, and eggs) and vegetable protein (cereals, legumes, soy products, and vegetables). Previous studies have demonstrated that the intake of vegetable

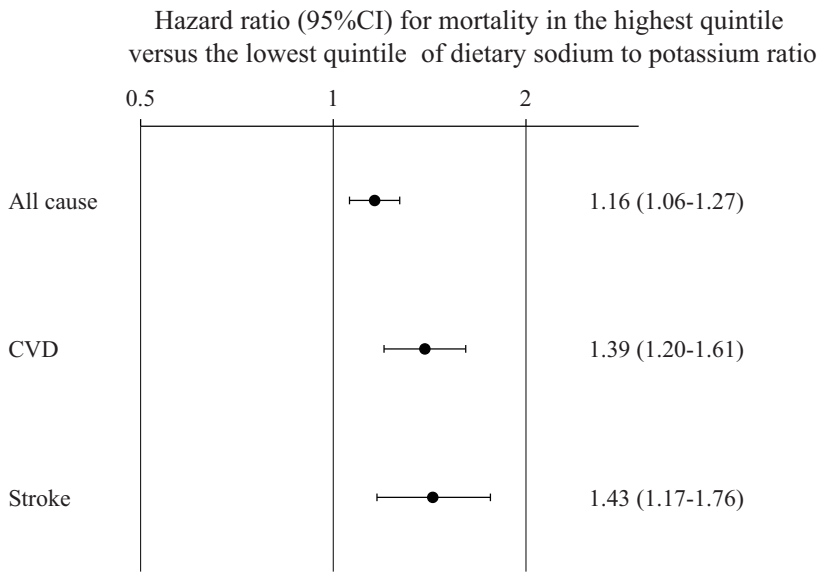

Fig. 4. HRs of mortality in the highest vs. the lowest quintile of dietary sodium-to-potassium ratio[63]

HRs were adjusted for age, sex, body mass index, smoking status, alcohol drinking, diabetes, serum total cholesterol, and intake of protein and fat (%kcal).

protein is inversely associated with blood pressure levels[64-66]. However, the association of the types of dietary protein with CVD risk remains unclear. Using 15-year follow-up data from NIPPON DATA90, Kurihara *et al.* investigated the relationship between vegetable protein intake and CVD mortality[67]. Higher intake of vegetable protein was associated with lower intake of animal protein and total, animal, and vegetable fats. After adjustment for sex, age, BMI, and dietary intake, such as animal protein, total fat, sodium, and potassium, a 1% energy increment of vegetable protein was significantly associated with a lower risk of CVD (HR: 0.86, 95% CI: 0.75–0.99) and cerebral hemorrhage (HR: 0.58, 95% CI: 0.35–0.95) mortality. The proportion of vegetable protein to total protein in the Japanese population was higher than that reported in the Western population[68-70]. In a population with relatively higher intake of vegetable protein, the intake of vegetable protein may be inversely related to CVD mortality risk. The intake of vegetable protein-rich foods, such as soy or soy products, may be recommended for preventing CVD.

3.5. Total Energy

In animal studies, dietary energy restriction has been indicated to reduce the risk of chronic diseases, such as cancer, hypertension, and diabetes[71-73], and also to increase lifespan[74], whereas studies on humans remain inconclusive[75]. We investigated the association between total energy intake and long-term total and cause-specific mortality risk, including cancer and CVD, in NIPPON DATA80 [76]. In men, the multivariable-adjusted HR for total mortality was higher in the highest quintile of total energy intake compared with that in the lowest quintile (HR: 1.45, 95% CI: 1.12–1.86, *P* for trend=0.008), whereas no such association was observed in women (HR: 0.90, 95% CI: 0.68–1.20, *P* for trend=0.527). In the cause-specific analysis, the mortality risk in the highest quintile of total energy intake was higher for CHD in both men (HR: 2.63, 95% CI: 0.95–7.28, *P* for trend=0.016) and women (HR: 2.91, 95% CI: 1.02–8.29, *P* for trend=0.032) and for cancer in men (HR: 1.50, 95% CI: 0.999–2.24, *P* for trend=0.038), compared with that in the lowest quintile. These findings partially support animal evidence and imply that energy restriction could decrease the risk of mortality in humans.

4. Association of Dietary Pattern in Japan with Cardiovascular Risk

4.1. Japanese Dietary Pattern

The Japanese people are well known to have long life expectancy[77], and the Japanese dietary pattern has received special attention as a contributing factor to this longevity. The traditional Japanese diet is characterized by higher fish intake and lower fat intake, which may lower the risk of CHD. A disadvantage of this diet is the high salt intake, which may lead to hypertension and a higher risk of stroke.

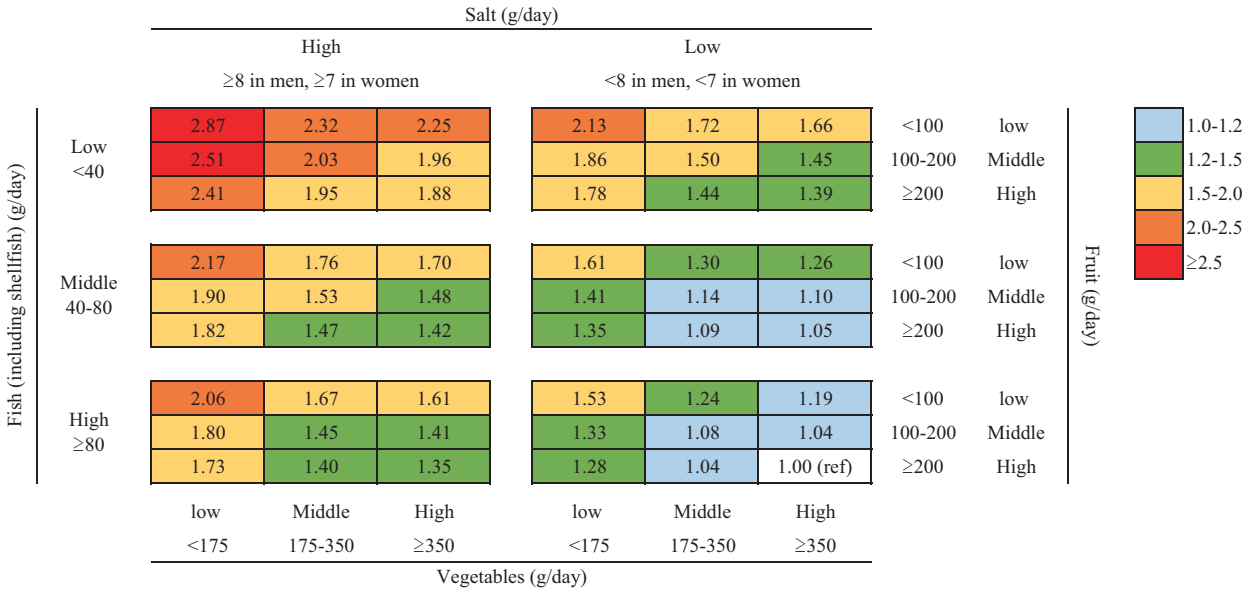

Fig. 5. Risk assessment chart for CVD mortality according to dietary factors[82)]

The HR for cardiovascular disease mortality according to the dietary intake of a combination of factors (vegetables, fruits, fish, and salt) was calculated by multiplying together the HRs for each of the dietary factors.

Accordingly, if the Japanese diet is modified to emphasize less-salty foods, Japanese longevity might increase further. Our research group investigated the relationships between a healthy reduced-salt Japanese diet and total and cause-specific mortality risk using 19-year follow-up data from NIPPON DATA80 [78)]. In this study, a healthy dietary score was created using seven dietary components to measure a healthy reduced-salt Japanese diet. The components included egg intake ≤ 2 eggs/week, fish intake once or more every 2 days, meat intake ≤ 2 times/week, tsukemono (salted pickles) intake once or more daily, infrequent intake of soup with noodles, use of low-salt soy sauce, and drinking alcohol only occasionally. Because data on absolute salt intake were not available in this study, infrequent intake of soup with noodles and use of low-salt soy sauce were used as markers for salt restriction. If any single dietary component was part of a typical daily diet, it was scored as 1 and 0 otherwise. The range of total score was from 0 to 7, with 0 being least healthy and 7 the healthiest. The participants were divided into tertiles of dietary scores (0–2, 3, and 4–7). After adjustment for age, sex, BMI, and other risk factors, the HRs for the highest score group (4–7), compared with those for the lowest score group (0–2), were 0.78 (95% CI: 0.70–0.88, *P* for trend<0.0001) for total mortality, 0.75 (95% CI: 0.56–0.99, *P* for trend=0.038) for stroke mortality, and 0.80 (95% CI: 0.66–0.97, *P* for trend=0.022) for CVD mortality. Adherence to a healthy reduced-salt Japanese diet was associated with a lower risk of CVD mortality. Although high salt intake is one disadvantage of the traditional Japanese diet, salt intake in Japan has significantly decreased over the past several decades, and this reduction may be one explanation for reducing stroke mortality. This is consistent with our findings, suggesting that a Japanese diet with reduced salt would prevent CVD and stroke and could lead to increased longevity. In contrast, the intake of potassium and calcium in Japan is low compared with that in Western countries, which is one of characteristics on Japanese dietary pattern. However, information regarding the intake of potassium and calcium was not available during the publication of this paper, which is one of the study limitations.

4.2. CVD Risk Assessment Chart by Dietary Factors

Many prospective cohort studies, including the NIPPON DATA study, have found associations between dietary factors and CVD risk. In particular, higher intake of fruit[7, 13, 79, 80)], vegetables[7, 13, 79, 80)], and fish[16, 42, 45)] and lower intake of salt[55, 58, 63, 81)] have been shown to be related to lower risk of CVD. However, most previous studies have reported on an association between a single dietary factor and CVD risk, although adjustments were made for other factors. Normally, humans ingest multiple foods combined, rather than a single food or nutrient, making it necessary to evaluate CVD risk by a combination of

dietary factors. We therefore studied the relationships between the combination of dietary factors and CVD mortality risk and also created a risk assessment chart for CVD mortality by these factors using 29-year follow-up data from NIPPON DATA80 [82]. In this study, the intake levels of vegetables, fruits, fish, and salt were used and classified into two or three categories based on the cutoff values from the Japanese government dietary guidelines[20, 83, 84]. The risk of CVD mortality was significantly higher in the lowest intake category compared with that in the highest intake category for vegetables (HR: 1.28, 95% CI: 1.04–1.58), fruits (HR: 1.19, 95% CI: 1.02–1.40), and fish (HR: 1.39, 95% CI: 1.10–1.77). Compared with lower salt intake, higher salt intake was also related to a higher risk of CVD mortality (HR: 1.35, 95% CI: 1.02–1.79). By multiplying the HRs of CVD mortality for each dietary factor together, we constructed a risk assessment chart for CVD mortality according to the dietary factors **(Fig. 5)**. The weighed dietary records used in this study can directly assess the absolute intake of salt. Thus, from this assessment chart, for example, a higher intake of vegetables, fruits, and fish were found to be associated with a lower risk of CVD mortality in both the higher and lower salt intake groups. This chart could be useful for a nutritional education on the prevention of CVD in the Japanese population.

5. Conclusions

We reviewed the findings on food and nutrient intake, dietary patterns, and CVD mortality risk reported from the NIPPON DATA80/90 study. These findings indicate that a dietary pattern high in fruit, vegetables, fish (n-3 PUFA), and dietary fiber and low in salt and sodium-to-potassium ratio is recommended for preventing CVD. This combination of dietary factors (fruits, vegetables, fish, and salt) was also associated with variation in CVD mortality risk, and we constructed a CVD risk assessment chart according to such dietary factors. We hope that this review would be useful for developing effective strategies for preventing CVD and would lead to further research in Japan, other Asian countries, and worldwide.

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Conflicts of Interest

The authors declare no conflict of interest.

References

1) Nippon Data 80 Research Group: Impact of elevated blood pressure on mortality from all causes, cardiovascular diseases, heart disease and stroke among Japanese: 14 year follow-up of randomly selected population from Japanese -- Nippon data 80. J Hum Hypertens, 2003; 17: 851-857
2) Ueshima H, Choudhury SR, Okayama A, Hayakawa T, Kita Y, Kadowaki T, Okamura T, Minowa M and Iimura O: Cigarette smoking as a risk factor for stroke death in Japan: NIPPON DATA80. Stroke, 2004; 35: 1836-1841

3) NIPPON DATA80 Research Group: Risk assessment chart for death from cardiovascular disease based on a 19-year follow-up study of a Japanese representative population. Circ J, 2006; 70: 1249-1255
4) Okuda N, Miura K, Yoshita K, Matsumura Y, Okayama A, Nakamura Y, Okamura T, Saitoh S, Sakata K, Ojima T, Turin TC and Ueshima H: Integration of data from NIPPON DATA80/90 and National Nutrition Survey in Japan: for cohort studies of representative Japanese on nutrition. J Epidemiol, 2010; 20 Suppl 3: S506-514
5) Yoshiike N, Matsumura Y, Iwaya M, Sugiyama M and Yamaguchi M: National Nutrition Survey in Japan. J Epidemiol, 1996; 6: S189-200
6) Okamura T, Hayakawa T, Kadowaki T, Kita Y, Okayama A, Elliott P and Ueshima H: Resting heart rate and cause-specific death in a 16.5-year cohort study of the Japanese general population. Am Heart J, 2004; 147: 1024-1032
7) Crowe FL, Roddam AW, Key TJ, Appleby PN, Overvad K, Jakobsen MU, Tjønneland A, Hansen L, Boeing H, Weikert C, Linseisen J, Kaaks R, Trichopoulou A, Misirli G, Lagiou P, Sacerdote C, Pala V, Palli D, Tumino R, Panico S, Bueno-de-Mesquita HB, Boer J, van Gils CH, Beulens JW, Barricarte A, Rodríguez L, Larrañaga N, Sánchez MJ, Tormo MJ, Buckland G, Lund E, Hedblad B, Melander O, Jansson JH, Wennberg P, Wareham NJ, Slimani N, Romieu I, Jenab M, Danesh J, Gallo V, Norat T and Riboli E: Fruit and vegetable intake and mortality from ischaemic heart disease: results from the European Prospective Investigation into Cancer and Nutrition (EPIC)-Heart study. Eur Heart J, 2011; 32: 1235-1243
8) Streppel MT, Sluik D, van Yperen JF, Geelen A, Hofman A, Franco OH, Witteman JC and Feskens EJ: Nutrient-rich foods, cardiovascular diseases and all-cause mortality: the Rotterdam study. Eur J Clin Nutr, 2014; 68: 741-747
9) Oyebode O, Gordon-Dseagu V, Walker A and Mindell JS: Fruit and vegetable consumption and all-cause, cancer and CVD mortality: analysis of Health Survey for England data. J Epidemiol Community Health, 2014; 68: 856-862
10) Aune D, Giovannucci E, Boffetta P, Fadnes LT, Keum N, Norat T, Greenwood DC, Riboli E, Vatten LJ and Tonstad S: Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies. Int J Epidemiol, 2017; 46: 1029-1056
11) Gan Y, Tong X, Li L, Cao S, Yin X, Gao C, Herath C, Li W, Jin Z, Chen Y and Lu Z: Consumption of fruit and vegetable and risk of coronary heart disease: a meta-analysis of prospective cohort studies. Int J Cardiol, 2015; 183: 129-137
12) Hu D, Huang J, Wang Y, Zhang D and Qu Y: Fruits and vegetables consumption and risk of stroke: a meta-analysis of prospective cohort studies. Stroke, 2014; 45: 1613-1619
13) Okuda N, Miura K, Okayama A, Okamura T, Abbott RD, Nishi N, Fujiyoshi A, Kita Y, Nakamura Y, Miyagawa N, Hayakawa T, Ohkubo T, Kiyohara Y and Ueshima H: Fruit and vegetable intake and mortality from cardiovascular disease in Japan: a 24-year follow-up of the NIPPON DATA80 Study. Eur J Clin Nutr, 2015; 69: 482-488
14) Takachi R, Inoue M, Ishihara J, Kurahashi N, Iwasaki M, Sasazuki S, Iso H, Tsubono Y and Tsugane S: Fruit and vegetable intake and risk of total cancer and cardiovascular disease: Japan Public Health Center-Based Prospective Study. Am J Epidemiol, 2008; 167: 59-70
15) Nagura J, Iso H, Watanabe Y, Maruyama K, Date C, Toyoshima H, Yamamoto A, Kikuchi S, Koizumi A, Kondo T, Wada Y, Inaba Y and Tamakoshi A: Fruit, vegetable and bean intake and mortality from cardiovascular disease among Japanese men and women: the JACC Study. Br J Nutr, 2009; 102: 285-292
16) Chowdhury R, Stevens S, Gorman D, Pan A, Warnakula S, Chowdhury S, Ward H, Johnson L, Crowe F, Hu FB and Franco OH: Association between fish consumption, long chain omega 3 fatty acids, and risk of cerebrovascular disease: systematic review and meta-analysis. Bmj, 2012; 345: e6698
17) Iso H, Sato S, Folsom AR, Shimamoto T, Terao A, Munger RG, Kitamura A, Konishi M, Iida M and Komachi Y: Serum fatty acids and fish intake in rural Japanese, urban Japanese, Japanese American and Caucasian American men. Int J Epidemiol, 1989; 18: 374-381
18) Ueshima H, Stamler J, Elliott P, Chan Q, Brown IJ, Carnethon MR, Daviglus ML, He K, Moag-Stahlberg A, Rodriguez BL, Steffen LM, Van Horn L, Yarnell J and Zhou B: Food omega-3 fatty acid intake of individuals (total, linolenic acid, long-chain) and their blood pressure: INTERMAP study. Hypertension, 2007; 50: 313-319
19) Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Tamaki S and Okayama A: Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980-99. Am J Med, 2005; 118: 239-245
20) Yoshiike N, Hayashi F, Takemi Y, Mizoguchi K and Seino F: A new food guide in Japan: the Japanese food guide Spinning Top. Nutr Rev, 2007; 65: 149-154
21) Ministry of Health, Labour and Welfare of Japan: The dietary reference intakes for Japanese, 2020. https: // wwwmhlwgojp/stf/seisakunitsuite/bunya/kenkou_iryou/kenkou/eiyou/syokuji_kijyunhtml (accessed April 3, 2022) (in Japanese)
22) Ministry of Health and Welfare, Japan: The National Health and Nutrition Survey in Japan, 2019. Tokyo: Daiichi Shuppan; 2021 (in Japanese)
23) Bonthuis M, Hughes MC, Ibiebele TI, Green AC and van der Pols JC: Dairy consumption and patterns of mortality of Australian adults. Eur J Clin Nutr, 2010; 64: 569-577
24) Ness AR, Smith GD and Hart C: Milk, coronary heart disease and mortality. J Epidemiol Community Health, 2001; 55: 379-382
25) Elwood PC, Strain JJ, Robson PJ, Fehily AM, Hughes J, Pickering J and Ness A: Milk consumption, stroke, and heart attack risk: evidence from the Caerphilly cohort of older men. J Epidemiol Community Health, 2005; 59: 502-505
26) Umesawa M, Iso H, Date C, Yamamoto A, Toyoshima H, Watanabe Y, Kikuchi S, Koizumi A, Kondo T, Inaba Y, Tanabe N and Tamakoshi A: Dietary intake of calcium in relation to mortality from cardiovascular disease: the

JACC Study. Stroke, 2006; 37: 20-26
27) Umesawa M, Iso H, Ishihara J, Saito I, Kokubo Y, Inoue M and Tsugane S: Dietary calcium intake and risks of stroke, its subtypes, and coronary heart disease in Japanese: the JPHC Study Cohort I. Stroke, 2008; 39: 2449-2456
28) Kondo I, Ojima T, Nakamura M, Hayasaka S, Hozawa A, Saitoh S, Ohnishi H, Akasaka H, Hayakawa T, Murakami Y, Okuda N, Miura K, Okayama A and Ueshima H: Consumption of dairy products and death from cardiovascular disease in the Japanese general population: the NIPPON DATA80. J Epidemiol, 2013; 23: 47-54
29) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). Jama, 2001; 285: 2486-2497
30) Dawber TR, Nickerson RJ, Brand FN and Pool J: Eggs, serum cholesterol, and coronary heart disease. Am J Clin Nutr, 1982; 36: 617-625
31) Hu FB, Stampfer MJ, Rimm EB, Manson JE, Ascherio A, Colditz GA, Rosner BA, Spiegelman D, Speizer FE, Sacks FM, Hennekens CH and Willett WC: A prospective study of egg consumption and risk of cardiovascular disease in men and women. Jama, 1999; 281: 1387-1394
32) Ueshima H, Iida M, Shimamoto T, Konishi M, Tanigaki M, Doi M, Nakanishi N, Takayama Y, Ozawa H and Komachi Y: Dietary intake and serum total cholesterol level: their relationship to different lifestyles in several Japanese populations. Circulation, 1982; 66: 519-526
33) Nakamura Y, Okamura T, Tamaki S, Kadowaki T, Hayakawa T, Kita Y, Okayama A and Ueshima H: Egg consumption, serum cholesterol, and cause-specific and all-cause mortality: the National Integrated Project for Prospective Observation of Non-communicable Disease and Its Trends in the Aged, 1980 (NIPPON DATA80). Am J Clin Nutr, 2004; 80: 58-63
34) Nakamura Y, Okamura T, Kita Y, Okuda N, Kadota A, Miura K, Okayama A and Ueshima H: Re-evaluation of the associations of egg intake with serum total cholesterol and cause-specific and total mortality in Japanese women. Eur J Clin Nutr, 2018; 72: 841-847
35) Ministry of Health and Walfare: Manual for Health Examination under Health and Medical Service Law for the Elderly (in Japanese). Tokyo: Japan Public Health Association; 1987
36) McNamara DJ: The impact of egg limitations on coronary heart disease risk: do the numbers add up? J Am Coll Nutr, 2000; 19: 540s-548s
37) Anderson JW and Bush HM: Soy protein effects on serum lipoproteins: a quality assessment and meta-analysis of randomized, controlled studies. J Am Coll Nutr, 2011; 30: 79-91
38) Zhan S and Ho SC: Meta-analysis of the effects of soy protein containing isoflavones on the lipid profile. Am J Clin Nutr, 2005; 81: 397-408
39) Li SH, Liu XX, Bai YY, Wang XJ, Sun K, Chen JZ and Hui RT: Effect of oral isoflavone supplementation on vascular endothelial function in postmenopausal women: a meta-analysis of randomized placebo-controlled trials. Am J Clin Nutr, 2010; 91: 480-486
40) Nguyen HN, Miyagawa N, Miura K, Okuda N, Yoshita K, Arai Y, Nakagawa H, Sakata K, Ojima T, Kadota A, Takashima N, Fujiyoshi A, Ohkubo T, Abbott RD, Okamura T, Okayama A and Ueshima H: Dietary tofu intake and long-term risk of death from stroke in a general population. Clin Nutr, 2018; 37: 182-188
41) Jonas M, Reicher-Reiss H, Boyko V, Behar S and Grossman E: Hospital and 1-year outcome after acute myocardial infarction in patients with diabetes mellitus and hypertension. J Hum Hypertens, 2003; 17: 665-670
42) Iso H, Kobayashi M, Ishihara J, Sasaki S, Okada K, Kita Y, Kokubo Y and Tsugane S: Intake of fish and n3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-Based (JPHC) Study Cohort I. Circulation, 2006; 113: 195-202
43) Yamagishi K, Iso H, Date C, Fukui M, Wakai K, Kikuchi S, Inaba Y, Tanabe N and Tamakoshi A: Fish, omega-3 polyunsaturated fatty acids, and mortality from cardiovascular diseases in a nationwide community-based cohort of Japanese men and women the JACC (Japan Collaborative Cohort Study for Evaluation of Cancer Risk) Study. J Am Coll Cardiol, 2008; 52: 988-996
44) Anderson CA, Appel LJ, Okuda N, Brown IJ, Chan Q, Zhao L, Ueshima H, Kesteloot H, Miura K, Curb JD, Yoshita K, Elliott P, Yamamoto ME and Stamler J: Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. J Am Diet Assoc, 2010; 110: 736-745
45) Miyagawa N, Miura K, Okuda N, Kadowaki T, Takashima N, Nagasawa SY, Nakamura Y, Matsumura Y, Hozawa A, Fujiyoshi A, Hisamatsu T, Yoshita K, Sekikawa A, Ohkubo T, Abbott RD, Okamura T, Okayama A and Ueshima H: Long-chain n-3 polyunsaturated fatty acids intake and cardiovascular disease mortality risk in Japanese: a 24-year follow-up of NIPPON DATA80. Atherosclerosis, 2014; 232: 384-389
46) Kris-Etherton PM, Harris WS and Appel LJ: Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. Circulation, 2002; 106: 2747-2757
47) Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM and Brinkley LJ: Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med, 2000; 342: 1392-1398
48) Reynolds A, Mann J, Cummings J, Winter N, Mete E and Te Morenga L: Carbohydrate quality and human health: a series of systematic reviews and meta-analyses. Lancet, 2019; 393: 434-445
49) Ho HVT, Jovanovski E, Zurbau A, Blanco Mejia S, Sievenpiper JL, Au-Yeung F, Jenkins AL, Duvnjak L, Leiter L and Vuksan V: A systematic review and meta-analysis of randomized controlled trials of the effect of konjac glucomannan, a viscous soluble fiber, on LDL cholesterol and the new lipid targets non-HDL cholesterol and apolipoprotein B. Am J Clin Nutr, 2017; 105: 1239-1247
50) Whelton SP, Hyre AD, Pedersen B, Yi Y, Whelton PK and He J: Effect of dietary fiber intake on blood pressure: a meta-analysis of randomized, controlled clinical trials. J Hypertens, 2005; 23: 475-481

51) Threapleton DE, Greenwood DC, Evans CE, Cleghorn CL, Nykjaer C, Woodhead C, Cade JE, Gale CP and Burley VJ: Dietary fibre intake and risk of cardiovascular disease: systematic review and meta-analysis. Bmj, 2013; 347: f6879
52) Threapleton DE, Greenwood DC, Evans CE, Cleghorn CL, Nykjaer C, Woodhead C, Cade JE, Gale CP and Burley VJ: Dietary fiber intake and risk of first stroke: a systematic review and meta-analysis. Stroke, 2013; 44: 1360-1368
53) Miyazawa I, Miura K, Miyagawa N, Kondo K, Kadota A, Okuda N, Fujiyoshi A, Chihara I, Nakamura Y, Hozawa A, Nakamura Y, Kita Y, Yoshita K, Okamura T, Okayama A and Ueshima H: Relationship between carbohydrate and dietary fibre intake and the risk of cardiovascular disease mortality in Japanese: 24-year follow-up of NIPPON DATA80. Eur J Clin Nutr, 2020; 74: 67-76
54) Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, Appel LJ and Whelton PK: Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). Bmj, 2007; 334: 885-888
55) Strazzullo P, D'Elia L, Kandala NB and Cappuccio FP: Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. Bmj, 2009; 339: b4567
56) Mozaffarian D, Fahimi S, Singh GM, Micha R, Khatibzadeh S, Engell RE, Lim S, Danaei G, Ezzati M and Powles J: Global sodium consumption and death from cardiovascular causes. N Engl J Med, 2014; 371: 624-634
57) Aburto NJ, Ziolkovska A, Hooper L, Elliott P, Cappuccio FP and Meerpohl JJ: Effect of lower sodium intake on health: systematic review and meta-analyses. Bmj, 2013; 346: f1326
58) Shima A, Miyamatsu N, Miura K, Miyagawa N, Okuda N, Yoshita K, Kadota A, Suzuki H, Kondo K, Okamura T, Okayama A and Ueshima H: Relationship of household salt intake level with long-term all-cause and cardiovascular disease mortality in Japan: NIPPON DATA80. Hypertens Res, 2020; 43: 132-139
59) Asakura K, Uechi K, Masayasu S and Sasaki S: Sodium sources in the Japanese diet: difference between generations and sexes. Public Health Nutr, 2016; 19: 2011-2023
60) Zhao F, Zhang P, Zhang L, Niu W, Gao J, Lu L, Liu C and Gao X: Consumption and sources of dietary salt in family members in Beijing. Nutrients, 2015; 7: 2719-2730
61) Rose G and Stamler J: The INTERSALT study: background, methods and main results. INTERSALT Co-operative Research Group. J Hum Hypertens, 1989; 3: 283-288
62) Stamler J, Elliott P, Dennis B, Dyer AR, Kesteloot H, Liu K, Ueshima H and Zhou BF: INTERMAP: background, aims, design, methods, and descriptive statistics (nondietary). J Hum Hypertens, 2003; 17: 591-608
63) Okayama A, Okuda N, Miura K, Okamura T, Hayakawa T, Akasaka H, Ohnishi H, Saitoh S, Arai Y, Kiyohara Y, Takashima N, Yoshita K, Fujiyoshi A, Zaid M, Ohkubo T and Ueshima H: Dietary sodium-to-potassium ratio as a risk factor for stroke, cardiovascular disease and all-cause mortality in Japan: the NIPPON DATA80 cohort study. BMJ Open, 2016; 6: e011632
64) Stamler J, Caggiula A, Grandits GA, Kjelsberg M and Cutler JA: Relationship to blood pressure of combinations of dietary macronutrients. Findings of the Multiple Risk Factor Intervention Trial (MRFIT). Circulation, 1996; 94: 2417-2423
65) Stamler J, Elliott P, Kesteloot H, Nichols R, Claeys G, Dyer AR and Stamler R: Inverse relation of dietary protein markers with blood pressure. Findings for 10,020 men and women in the INTERSALT Study. INTERSALT Cooperative Research Group. INTERnational study of SALT and blood pressure. Circulation, 1996; 94: 1629-1634
66) Cirillo M, Lombardi C, Laurenzi M and De Santo NG: Relation of urinary urea to blood pressure: interaction with urinary sodium. J Hum Hypertens, 2002; 16: 205-212
67) Kurihara A, Okamura T, Sugiyama D, Higashiyama A, Watanabe M, Okuda N, Kadota A, Miyagawa N, Fujiyoshi A, Yoshita K, Ohkubo T, Okayama A, Miura K and Ueshima H: Vegetable Protein Intake was Inversely Associated with Cardiovascular Mortality in a 15-Year Follow-Up Study of the General Japanese Population. J Atheroscler Thromb, 2019; 26: 198-206
68) Altorf-van der Kuil W, Engberink MF, Vedder MM, Boer JM, Verschuren WM and Geleijnse JM: Sources of dietary protein in relation to blood pressure in a general Dutch population. PLoS One, 2012; 7: e30582
69) Haring B, Misialek JR, Rebholz CM, Petruski-Ivleva N, Gottesman RF, Mosley TH and Alonso A: Association of Dietary Protein Consumption With Incident Silent Cerebral Infarcts and Stroke: The Atherosclerosis Risk in Communities (ARIC) Study. Stroke, 2015; 46: 3443-3450
70) Ozawa M, Yoshida D, Hata J, Ohara T, Mukai N, Shibata M, Uchida K, Nagata M, Kitazono T, Kiyohara Y and Ninomiya T: Dietary Protein Intake and Stroke Risk in a General Japanese Population: The Hisayama Study. Stroke, 2017; 48: 1478-1486
71) Weindruch R, Walford RL, Fligiel S and Guthrie D: The retardation of aging in mice by dietary restriction: longevity, cancer, immunity and lifetime energy intake. J Nutr, 1986; 116: 641-654
72) Colman RJ, Anderson RM, Johnson SC, Kastman EK, Kosmatka KJ, Beasley TM, Allison DB, Cruzen C, Simmons HA, Kemnitz JW and Weindruch R: Caloric restriction delays disease onset and mortality in rhesus monkeys. Science, 2009; 325: 201-204
73) Weindruch R and Sohal RS: Seminars in medicine of the Beth Israel Deaconess Medical Center. Caloric intake and aging. N Engl J Med, 1997; 337: 986-994
74) Alcaín FJ and Villalba JM: Sirtuin activators. Expert Opin Ther Pat, 2009; 19: 403-414
75) Goto S: Health span extension by later-life caloric or dietary restriction: a view based on rodent studies. Biogerontology, 2006; 7: 135-138
76) Nagai M, Ohkubo T, Miura K, Fujiyoshi A, Okuda N, Hayakawa T, Yoshita K, Arai Y, Nakagawa H, Nakamura K, Miyagawa N, Takashima N, Kadota A, Murakami Y,

Nakamura Y, Abbott RD, Okamura T, Okayama A and Ueshima H: Association of Total Energy Intake with 29-Year Mortality in the Japanese: NIPPON DATA80. J Atheroscler Thromb, 2016; 23: 339-354
77) Ikeda N, Saito E, Kondo N, Inoue M, Ikeda S, Satoh T, Wada K, Stickley A, Katanoda K, Mizoue T, Noda M, Iso H, Fujino Y, Sobue T, Tsugane S, Naghavi M, Ezzati M and Shibuya K: What has made the population of Japan healthy? Lancet, 2011; 378: 1094-1105
78) Nakamura Y, Ueshima H, Okamura T, Kadowaki T, Hayakawa T, Kita Y, Abbott RD and Okayama A: A Japanese diet and 19-year mortality: national integrated project for prospective observation of non-communicable diseases and its trends in the aged, 1980. Br J Nutr, 2009; 101: 1696-1705
79) Bazzano LA, He J, Ogden LG, Loria CM, Vupputuri S, Myers L and Whelton PK: Fruit and vegetable intake and risk of cardiovascular disease in US adults: the first National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Am J Clin Nutr, 2002; 76: 93-99
80) Dauchet L, Amouyel P, Hercberg S and Dallongeville J: Fruit and vegetable consumption and risk of coronary heart disease: a meta-analysis of cohort studies. J Nutr, 2006; 136: 2588-2593
81) Takachi R, Inoue M, Shimazu T, Sasazuki S, Ishihara J, Sawada N, Yamaji T, Iwasaki M, Iso H, Tsubono Y and Tsugane S: Consumption of sodium and salted foods in relation to cancer and cardiovascular disease: the Japan Public Health Center-based Prospective Study. Am J Clin Nutr, 2010; 91: 456-464
82) Kondo K, Miura K, Tanaka-Mizuno S, Kadota A, Arima H, Okuda N, Fujiyoshi A, Miyagawa N, Yoshita K, Okamura T, Okayama A and Ueshima H: Cardiovascular Risk Assessment Chart by Dietary Factors in Japan - NIPPON DATA80. Circ J, 2019; 83: 1254-1260
83) Hishida A. Sasaki S. Dietary reference intakes for Japanese, 2015. Tokyo: Daiichishuppan, 2014
84) Japan Health Promotion and Fitness Foundation. Health Japan 21. Ministry of Health, Labor and Welfare. Report on Health Japan 21 Plan Study Committee and Health Japan 21 Plan Development Committee. Tokyo: Available at: http: //www. kenkounippon21.gr.jp/ (accessed April 3, 2022) (in Japanese)