日本食スコアにより分けた3群の死亡率の解析結果　男4,018人、女5,068人、-----NIPPON DATA80: 1980-99----

	スコア0-2	スコア3	スコア4-7	傾向P
人年	46,790	53,772	56,495	
総死亡（計=1,823）	556	634	633	
年齢・性調整 HR	1	0.92 (0.83-1.04)	0.78 (0.70-0.88)	<0.0001
多変量調整 HR				
モデル 1	1	0.93 (0.83-1.04)	0.78 (0.69-0.87)	<0.0001
モデル 2	1	0.92 (0.83-1.04)	0.78 (0.70-0.88)	<0.0001
心血管死（小計=654）	200	220	234	
年齢・性調整 HR	1	0.90 (0.75-1.09)	0.80 (0.66-0.96)	0.017
多変量調整 HR				
モデル 1	1	0.91 (0.75-1.10)	0.79 (0.65-0.95)	0.014
モデル 2	1	0.91 (0.75-1.10)	0.80 (0.66-0.97)	0.022
脳卒中死（小計=299）	92	107	100	
年齢・性調整 HR	1	0.95 (0.72-1.26)	0.74 (0.56-0.99)	0.035
多変量調整 HR				
モデル 1	1	0.96 (0.73-1.27)	0.74 (0.56-0.98)	0.031
モデル 2	1	0.96 (0.72-1.27)	0.75 (0.56-0.99)	0.038
心筋梗塞死（小計=131）	40	42	49	
年齢・性調整 HR	1	0.83 (0.55-1.26)	0.85 (0.55-1.31)	0.39
多変量調整 HR				
モデル 1	1	0.86 (0.56-1.33)	0.82 (0.54-1.25)	0.37
モデル 2	1	0.85 (0.55-1.32)	0.84 (0.55-1.27)	0.42
癌死（小計=551）	166	190	195	
年齢・性調整 HR	1	0.86 (0.70-1.05)	0.94 (0.77-1.16)	0.14
多変量調整 HR				
モデル 1	1	0.85 (0.69-1.05)	0.95 (0.77-1.17)	0.12
モデル 2	1	0.95 (0.77-1.17)	0.95 (0.77-1.17)	0.13

ハザード比（HR）と 95% 信頼区間を示す。多変量解析モデル1:年齢、性、 BMI, 喫煙(生涯非喫煙、喫煙既往、現在喫煙 < 20 本/日, 現在喫煙 20～40 本/日, 現在喫煙≥ 41 本/日)により調整。モデル2: モデル1＋高血圧、糖尿病により調整。BMI=body mass index.

British Journal of Nutrition (2009), **101**, 1696–1705
doi:10.1017/S0007114508111503

British Journal of Nutrition

A Japanese diet and 19-year mortality: National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980

Yasuyuki Nakamura[1,2]*, Hirotsugu Ueshima[2], Tomonori Okamura[2], Takashi Kadowaki[2], Takehito Hayakawa[3], Yoshikuni Kita[2], Robert D. Abbott[2,4], Akira Okayama[5] and for National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980 Research Group

[1]*Cardiovascular Epidemiology, Kyoto Women's University, 35 Imakumano Kitahiyoshi-cho, Higashiyama-ku, Kyoto 605-8501, Japan*
[2]*Department of Health Science, Shiga University of Medical Science, Otsu City, Shiga, Japan*
[3]*Department of Hygiene and Preventive Medicine, Fukushima Medical University, Fukushima, Japan*
[4]*Department of Epidemiology and Biostatistics, University of Virginia School of Medicine, Charlottesville, VA, USA*
[5]*Department of Preventive Cardiology, National Cardiovascular Center, Suita City, Japan*

(Received 4 April 2008 – Revised 22 September 2008 – Accepted 24 September 2008 – First published online 20 November 2008)

Few studies have examined the association between Japanese diet and mortality outcomes. We analysed the relationship between a healthy Japanese diet and all-cause and cause-specific mortality using the database from the National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980. At baseline in 1980, data were collected on study participants aged ≧ 30 years from randomly selected areas in Japan. We defined a measure of a healthy reduced-salt Japanese diet based on seven components from FFQ. The total score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. Participants were divided into approximate tertiles of dietary scores (0–2, 3 and 4–7 scores). After excluding participants with co-morbidities, we followed 9086 participants (44 % men) for 19 years. There were 1823 all-cause and 654 cardiovascular deaths during the follow-up. With the dietary score group 0–2 serving as a reference, the Cox multivariate-adjusted hazard ratios for groups with scores 3 and 4–7 were 0·92 (95 % CI 0·83, 1·04) and 0·78 (95 % CI 0·70, 0·88) for all-cause mortality (trend $P<0·0001$), and 0·91 (95 % CI 0·75, 1·10) and 0·80 (95 % CI 0·66, 0·97) for cardiovascular mortality (trend $P=0·022$). Adherence to a healthy reduced-salt Japanese diet was associated with an approximate 20 % lower rate of all-cause and cardiovascular mortality.

Dietary pattern: Japanese diet: Cohort studies: Mortality

Recent interest in dietary patterns has spawned several studies of the associations between dietary patterns and longevity[1,2]. Japanese cuisine is based on combining staple foods, typically rice or noodles, with soup, and side dishes made from fish, meat, vegetable, tofu and the like, designed to add flavour to the staple food. These are typically flavoured with dashi stock, made with katsuobushi (dried skipjack tuna flakes), miso and soya sauce, and are usually low in fat and high in salt. Since Japan is an island nation, people eat much seafood. Meat eating has been relatively rare. The beneficial aspects of the traditional Japanese diet have been attributed to its low intake of SFA and a high intake of PUFA, especially from fish. Long-term benefits include lower mortality from CHD and from some cancers, which contribute at least in part to Japanese having the longest life expectancy in the world[3,4]. A drawback of the Japanese diet is its high intake of salt and its association with a higher incidence and mortality from stroke and gastric cancer[5–7]. Presumably, if the Japanese diet is modified to emphasise the intake of foods that are low in salt, Japanese longevity could be increased further.

In the present study, we studied the preference for Japanese or Western diets, and from these data and those based on the previous studies, we comprehensively extracted the beneficial components of the Japanese diet and derived a healthy Reduced-Salt Japanese Diet Score. We analysed the relationship between the diet score and all-cause and cause-specific mortality using the database of the National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980 (NIPPON DATA80). The database includes more than 10 000 participants from randomly selected regions in Japan, who were followed for 19 years[8–10].

Abbreviation: BP, blood pressure.

* **Corresponding author:** Yasuyuki Nakamura, fax +81 75 531 2162, email nakamury@kyoto-wu.ac.jp

Methods

Participants

The participants in this cohort were those in the 1980 National Survey on Circulatory Disorders[8]. A total of 10546 community-based participants aged 30 years and above in 300 randomly selected health districts throughout Japan participated in the survey, which consisted of history taking, physical examinations, blood tests and a self-administered questionnaire on lifestyle, including an essential nutritional survey by the food-frequency method. For the present study, the participants were followed up to 1999 (National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99). The overall population aged 30 years and above in the participating health districts was 13771. The participation rate was 76·6% (10546 of 13771) before exclusion for reasons mentioned later.

We reviewed the residence records of all the study participants for their vital status. In the cases of deaths, the causes were examined. To clarify the cause of death, we used the National Vital Statistics records. The underlying cause of death was coded according to the ninth International Classification of Disease for the National Vital Statistics until the end of 1994 and according to the tenth International Classification of Disease from the beginning of 1995. Deaths were confirmed in each district by computer matching of data from the National Vital Statistics records using the district, sex and dates of birth and death as key codes.

Participants were excluded from follow-up because of a past history of coronary disease, stroke or significant co-morbidities such as renal insufficiency (*n* 539), because of missing baseline data (*n* 51) or because of a loss to follow-up (*n* 870). The latter group was excluded because of the absence of a permanent address that was required for linking to National Vital Statistics records. The final sample comprised 9086 participants (4018 men and 5068 women). There were no significant differences between participants who were lost to follow-up and those who were included in the present study in terms of several risk factor characteristics. Therefore, the potential bias regarding the 870 participants lost to follow-up is thought to be negligible. Permission to use the National Vital Statistics records was obtained from the Management and Coordination Agency, Government of Japan. Approval for the present study was obtained from the Institutional Review Board of Shiga University of Medical Science for ethical issues (no. 12–18, 2000).

Biochemical and baseline examinations

The baseline surveys were conducted at public health centres. Baseline blood pressures (BP) were measured by trained research nurses using a standard mercury sphygmomanometer on the right arm of seated participants after at least 5 min of rest. Hypertension was defined as systolic BP $\geq$ 140 mmHg, diastolic BP $\geq$ 90 mmHg, or when a participant was receiving medications for the treatment of high BP. Height and weight were measured in stocking feet and light clothing. BMI was calculated as weight (kg) divided by the square of height (m^2).

A lifestyle survey was also carried out using a self-administered questionnaire that asked about the typical daily consumption of thirty-one food items, as shown in Appendix. Egg consumption was coded as $\geq$2 eggs/d, about 1 egg/d, about 1 egg/2 d, about 1–2 eggs/week and less than once per week. Fish, meat and tsukemono (preserved roots or leaves of seasonal vegetables, e.g. cucumbers and aubergine, which are consumed with rice at the end of a meal) intake was coded separately as $\geq$2 times/d, about 1 time/d, about 1 time/2 d, about 1–2 times/week and less than once per week. The participants were also asked whether they frequently consumed soup with noodles, whether they used low-salt soya sauce and what their preferred type of diet was (Japanese, Western or mixed; Q19 in Appendix). They were enquired about their alcohol drinking habit (never, past, occasional and daily drinkers). Reported information was confirmed by public health nurses through interviews with the study participants regarding food consumption, smoking, drinking habit and present and past medical histories.

Non-fasting blood samples were drawn and centrifuged within 60 min of collection and stored at −70°C until analyses. Serum total cholesterol, albumin, uric acid and creatinine were analysed in a sequential auto-analyser (SMA12/60, Technicon, Tarrytown, NY, USA) at a single laboratory (Osaka Medical Center for Health Science and Promotion). This laboratory is a member of the Cholesterol Reference Method Laboratory Network[11]. Serum concentrations of glucose were measured by the cupric-neocuproine method[12]. Diabetes was determined by medical history or defined as a serum glucose concentration $\geq$2000 mg/l.

Statistical analysis and components of the Reduced-Salt Japanese Diet Score

Statistical Analysis Systems statistical software package version 9.1 for Windows (SAS Institute, Cary, NC, USA) was used throughout the analyses. We examined the relationship between the type of preferred diet and the frequency of dietary components from the nutritional survey. Then, we defined seven components from the nutritional survey to measure a healthy reduced-salt Japanese diet. The components included egg intake $\leq$2 eggs/week, fish intake once or more often in 2 d, meat intake $\leq$2 times/week, tsukemono intake once or more often per day, infrequent intake of soup with noodles, use of low-salt soya sauce and occasional drinking. The afore-mentioned cut-off values were determined based on the previous studies on the intake of eggs, fish and alcohol[9,10,13–15]. For meat and tsukemono, a near median was used as the cut-off. Infrequent intake of soup with noodles and the use of low-salt soya sauce were used as markers of salt restriction. Because data on the amounts of alcohol consumed were not available, and the association between all-cause mortality and alcohol consumption is known to be J-shaped[15], we chose occasional drinking as a component of a healthy reduced-salt Japanese diet. Moderate alcohol consumption was also a component of a Mediterranean diet[2]. If any single dietary component was part of a typical daily diet, it was scored as 1 and 0 otherwise. Thus, the total score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. The participants were divided into approximate tertiles of dietary scores (0–2, 3 and 4–7 scores). To obtain trend *P*, the Mantel–Haenszel χ^2 statistical test was used to detect deviation from linearity

in the association between nominal variables and the categories according to the diet score, and the ANOVA was used to detect deviation from linearity in the association between continuous variables and the categories. To examine the association between the Reduced-Salt Japanese Diet Score and all-cause and cause-specific mortality, age -, sex- and multivariate-adjusted hazard ratios were calculated using a Cox proportional hazards model. For multivariate analyses, age, sex, BMI and cigarette smoking (never and past smokers, current smokers <20 cigarettes/d, current smokers 20–40 cigarettes/d and current smokers ≥41 cigarettes/d) were entered as covariates for model 1. For model 2, hypertension and diabetes were added. The dietary score group 0–2 served as a reference for comparison with the other tertiles. Sensitivity analyses were performed on the afore-mentioned Cox analysis by excluding those who did not report a preferred food type, by stratifying the lower and higher age groups at median age, 49·3 years, and by stratifying by sex. To examine the association between each of the components of a Reduced-Salt Japanese Diet Score and all-cause mortality, adjustments were made for the covariates in model 2.

To estimate adjusted survival probabilities, we derived Kaplan–Meier survival curves after propensity score matching[16]. Variables used in the propensity score were selected from the non-dietary variables: age (years), men (%), BMI (kg/m^2), current smokers (%), systolic BP (mmHg), diastolic BP (mmHg), on hypertension drugs (%), diabetes (%), serum total cholesterol (mg/l), albumin (mg/l), uric acid (mg/l) and creatinine (mg/l). After matching, adjusted survival curves were estimated separately for those participants who fell in the Japanese dietary grouping that ranged from 0 to 3 and for those in grouping strata 4 and higher. Comparison of the survival curves was based on the log-rank test. We further examined survival differences by the two groups according to the diet score, with age and sex as the dependent variables in a regression model. The statistical model used was a life table regression procedure, with a Weibull distribution assumption for failure time included. The variables used in the calculation of the propensity score were also compared by t test and χ^2 test to determine whether the propensity score matching was successful in mitigating risk factor differences.

Results

Baseline characteristics and all-cause mortality according to preferred food type

The baseline characteristics according to the preferred food type are shown in Table 1. In this table, we excluded 201 participants with missing data on a preferred food type. Relatively few participants preferred the Western food type. Participants in this group were younger, were more likely to be women and were less often hypertensive than participants who chose the other diet types. Those who preferred a Western type of diet ate meat more frequently and consumed fish and tsukemono less often than those in the other groups. The two markers of salt restriction (infrequent consumption of soup with noodles and the use of low-salt soya sauce) were more prevalent among those who preferred a Western diet. Small differences, but a significant trend in the Reduced-Salt Japanese Diet Score, were observed (trend $P<0·0001$).

Baseline characteristics according to Reduced-Salt Japanese Diet Score

Table 2 shows the baseline characteristics according to tertiles of the Reduced-Salt Japanese Diet Score. As the score increased, the mean age and BMI increased, although the latter increase was modest. The proportion of women and the prevalence of hypertension, daily drinking and non-smoking also increased with diet score. The prevalence of diabetes and the mean serum total cholesterol concentration were not significantly different across the groups. As expected, the percentage with each component of the Reduced-Salt Japanese Diet Score increased as the score increased.

Table 1. Baseline characteristics according to preferred food type – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Mean values and standard deviations)

	Japanese		Mixture		Western		
	Mean	SD	Mean	SD	Mean	SD	Trend *P*
Number at risk	6505		1977		403		
Age (years)	52·2	13·0	45·9	12·4	44·7	12·2	<0·0001
Men (%)	48·4		33·7		32·5		<0·0001
BMI (kg/m^2)	22·8	3·2	22·5	3·0	22·4	3·1	0·003
Hypertension (%)	47·8		36·2		31·8		<0·0001
Diabetes (%)	5·8		3·6		4·5		0·0002
Daily drinkers (%)	20·6		23·2		24·3		<0·0001
Current smokers (%)	35·8		25·7		23·1		<0·0001
Egg (/week)	4·0	2·8	4·0	2·7	4·0	2·7	0·42
Fish (times/week)	4·8	3·4	4·3	2·9	4·3	3·0	<0·0001
Meat (times/week)	3·5	2·7	4·3	3·0	4·7	3·3	<0·0001
Tsukemono (times/week)	9·6	5·0	8·3	5·2	6·6	5·0	<0·0001
Infrequent consumption of soup with noodles (%)	51·0		55·2		62·5		<0·0001
Use of low-salt soya sauce (%)	16·7		17·3		18·4		<0·0001
Reduced-Salt Japanese Diet Score	3·2	1·1	3·0	1·1	3·0	1·1	<0·0001

*We excluded 201 participants in this table, who did not choose their preferred food type. To obtain trend *P*s, the Mantel–Haenszel χ^2 statistical test was used for nominal variables, and the ANOVA for continuous variables.

Table 2. Baseline characteristics according to tertiles of the Reduced-Salt Japanese Diet Score among 4018 men and 5068 women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Mean values and standard deviations)

	Score 0–2		Score 3		Score 4–7		
	Mean	SD	Mean	SD	Mean	SD	Trend *P*
No. at risk (total = 9086)	2719		3113		3254		
Age (years)	49·1	13·5	50·7	13·1	51·7	13·0	<0·0001
Men (%)	49·3		43·6		40·5		<0·0001
BMI (kg/m^2)	22·6	3·0	22·7	3·2	22·8	3·2	0·003
Hypertension (%)	41·9		45·0		47·0		<0·0001
Diabetes (%)	4·6		5·6		5·4		0·18
Daily drinkers (%)	6·3		18·8		36·1		<0·0001
Current smokers (%)	35·4		32·2		31·5		<0·0001
TCH (mg/l)	1890	330	1890	340	1880	340	0·33
Egg ≤2 eggs/week (%)	10·1		29·5		60·3		<0·0001
Fish once or more often in 2 d (%)	26·2		35·0		38·8		<0·0001
Meat ≤2 times/week (%)	12·7		30·5		56·8		<0·0001
Tsukemono once or more often per day (%)	22·0		35·6		42·4		<0·0001
Infrequent consumption of soup with noodles (%)	12·3		34·4		53·3		<0·0001
Use of low-salt soya sauce (%)	6·5		23·0		70·6		<0·0001
Occasional drinking (%)	8·8		30·4		60·8		<0·0001

No., number; TCH, serum total cholesterol concentration.

*We defined a healthy Japanese diet based on seven components: egg intake ≤2 eggs/week, fish intake once or more often in 2 d, meat intake ≤2 times/week, tsukemono (preserved roots or leaves of seasonal vegetables) intake once or more often per day, infrequent intake of soup with noodles, use of low-salt soya sauce and occasional drinking. If a dietary component was part of a typical daily diet, it was scored as 1 and 0 otherwise. Thus, the total Reduced-Salt Japanese Diet Score ranged from 0 to 7, with 0 being least healthy and 7 being most healthy. To obtain trend *P*s, the Mantel–Haenszel χ^2 statistical test was used for nominal variables, and the ANOVA for continuous variables.

All-cause and cause-specific mortality according to Reduced-Salt Japanese Diet Score

During the 19 years of follow-up, there were 1823 deaths. In this group, 654 were from CVD, 299 from stroke, 131 acute myocardial infarction, 551 cancer and 119 non-cardiovascular, non-cancer inflammatory diseases[17]. Table 3 shows the total person-years, numbers of cases, hazard ratios and 95 % CI for all-cause and cause-specific mortality for each category of Reduced-Salt Japanese Diet Score after adjustment for age, sex and other risk factors (multivariate models 1 and 2). As the score increased, risk of death from all-cause mortality, CVD and stroke declined significantly in all models. Mortality from acute myocardial infarction, cancer and inflammatory diseases tended to decrease, but without statistical significance, a possible consequence of the relatively small number of such events. Similar results were observed after excluding participants with missing data on dietary preference. At high-age strata and in men, similar results were observed for all-cause mortality, CVD and stroke mortality. However, at low-age strata and in women, results were similar for all-cause mortality only. Significant differences by the groups according to the diet score were lost at low-age strata and in women for CVD and stroke mortality, probably because of the relatively smaller number of such events at low-age strata.

Components of Reduced-Salt Japanese Diet Score and all-cause mortality

The percentage of total participants who observed a healthy component of the Reduced-Salt Japanese Diet Score and the association of each component with all-cause mortality are shown in Table 4. The percentage of male participants who observed a healthy reduced-salt Japanese dietary component is also provided. Adherence to each of the healthy dietary components tended to be associated with lower mortality. Risk of death, however, was significantly lower for participants who ate tsukemono once or more often per day, consumed soup with noodles infrequently and drank alcohol occasionally.

Kaplan-Meier survival estimates after propensity score matching

The results from the propensity score matching are shown in Table 5. Fifty-eight participants with the Reduced-Salt Japanese Diet Score 4–7 were unmatched due to missing data (*n* 56) or failure to match on propensity scores (*n* 2). As can be seen, significant differences in the average propensity score and the variables used in its calculation before matching in the two groups disappeared after matching. By contrast, a significant difference between the matched survival curves remained as shown in Fig. 1 ($P=0·0003$ by log-rank test). Survival differences by the group were significant when examined further using a regression model with a Weibull distribution that included adjustment for age and sex as the dependent variables (estimate $= -0·13$ (the lower score group compared with the higher score group), $P<0·0001$).

Discussion

The cut-off values for the egg, fish and drinking components were determined based on the previous studies[11,12,18–23]. Near-median cut-off values were used for meat and tsukemono. The low intake of meat is one of the characteristic features of the traditional Japanese diet and serves as a marker of reduced intake of SFA in the Japanese[3,4,18,19]. Although frequent intake of tsukemono is also a character-

NS British Journal of Nutrition

Table 3. All-cause and cause-specific mortality according to Reduced-Salt Japanese Diet Score among 9089 men and women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Hazard ratios (HR) and 95% confidence intervals)

	Score 0–2	Score 3		Score 4–7		
		HR	95% CI	HR	95% CI	Trend *P*
Person-years	46790	53772		56495		
All-cause death (total = 1823)	556	634		633		
Age-, sex-adjusted HR	1	0·92	0·83, 1·04	0·78	0·70, 0·88	<0·0001
Multivariate HR						
Model 1	1	0·93	0·83, 1·04	0·78	0·69, 0·87	<0·0001
Model 2	1	0·92	0·83, 1·04	0·78	0·70, 0·88	<0·0001
CVD death (subtotal = 654)	200	220		234		
Age-, sex-adjusted HR	1	0·90	0·75, 1·09	0·80	0·66, 0·96	0·017
Multivariate HR						
Model 1	1	0·91	0·75, 1·10	0·79	0·65, 0·95	0·014
Model 2	1	0·91	0·75, 1·10	0·80	0·66, 0·97	0·022
Stroke death (subtotal = 299)	92	107		100		
Age-, sex-adjusted HR	1	0·95	0·72, 1·26	0·74	0·56, 0·99	0·035
Multivariate HR						
Model 1	1	0·96	0·73, 1·27	0·74	0·56, 0·98	0·031
Model 2	1	0·96	0·72, 1·27	0·75	0·56, 0·99	0·038
AMI death (subtotal = 131)	40	42		49		
Age-, sex-adjusted HR	1	0·83	0·55, 1·26	0·85	0·55, 1·31	0·39
Multivariate HR						
Model 1	1	0·86	0·56, 1·33	0·82	0·54, 1·25	0·37
Model 2	1	0·85	0·55, 1·32	0·84	0·55, 1·27	0·42
Cancer death (subtotal = 551)	166	190		195		
Age-, sex-adjusted HR	1	0·94	0·77, 1·16	0·86	0·70, 1·05	0·14
Multivariate HR						
Model 1	1	0·95	0·77, 1·17	0·85	0·69, 1·05	0·12
Model 2	1	0·95	0·77, 1·17	0·85	0·69, 1·05	0·13
Non-CVD, non-cancer, Inflam. death (subtotal = 119)	40	37		42		
Age-, sex-adjusted HR	1	0·81	0·52, 1·27	0·74	0·48, 1·14	0·18
Multivariate HR						
Model 1	1	0·80	0·51, 1·25	0·74	0·48, 1·13	0·17
Model 2	1	0·80	0·51, 1·25	0·74	0·48, 1·14	0·18

AMI, acute myocardial infarction; Inflam., inflammatory disease.
*Multivariate, multivariate-adjusted Cox analysis. Model 1: adjusted for age, sex, BMI and smoking (never and ex-smokers, current smokers < 20 cigarettes/d, current smokers 20–40 cigarettes/d and current smokers ≥41 cigarettes/d). Model 2: adjusted for model 1 covariates plus hypertension and diabetes.

istic feature of the traditional Japanese diet, it was unexpected to find that consuming tsukemono at least once a day was associated with a statistically significant lower risk of all-cause mortality. Many types of Japanese tsukemono are prepared in a traditional Japanese fashion with high reliance on salt. It may be, however, that the more healthy nutrient content of tsukemono outweighs the adverse consequences from consuming tsukemono with high sodium content. Conversely, the healthy nutritional value from eating unsalted tsukemono may be modest and offer little prognostic significance. Rather, its association with lower mortality may be through a high likelihood of being associated with a traditional Japanese diet. Those who eat tsukemono may consume meat less often and prefer foods that are commonly enjoyed with tsukemono, such as fish, vegetables, fruits and soya bean products.

Table 4. Components of Reduced-Salt Japanese Diet Score and all-cause mortality among 9089 men and women – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99*

(Hazard ratios (HR) and 95% confidence intervals)

Component	Total (%)	Men %	HR	95% CI	*P*
Egg ≤2 eggs/week	36·1	40·0	0·93	0·84, 1·02	0·11
Fish once or more often in 2 d	71·9	45·9	0·98	0·88, 1·08	0·67
Meat ≤2 times/week	38·1	40·6	0·97	0·88, 1·06	0·51
Tsukemono once or more often per day	77·0	43·8	0·89	0·80, 0·998	0·045
Infrequent consumption of soup with noodles	51·3	36·3	0·88	0·80, 0·97	0·007
Use of low-salt soya sauce	16·6	41·8	0·99	0·88, 1·12	0·86
Occasional drinking	21·2	55·4	0·81	0·71, 0·92	0·001

Total (%), percentage of total participants who had each component of Reduced-Salt Japanese Diet Score; men %, percentage of men who had each component.
*Multivariate, multivariate-adjusted Cox analysis adjusted for age, sex, BMI, hypertension, diabetes and smoking (never and ex-smokers, current smokers <20 cigarettes/d, current smokers 20–40 cigarettes/d and >40 cigarettes/d).

NS British Journal of Nutrition

Table 5. Variables used for propensity score matching and survival rate – National Integrated Project for Prospective Observation of Non-Communicable Diseases and its Trends in the Aged, 1980, 1980–99

(Mean values and standard deviations)

	Before matching					After matching				
	Score 4–7		Score 0–3			Score 4–7		Score 0–3		
	Mean	SD	Mean	SD	*P*	Mean	SD	Mean	SD	*P*
n	3254		5832			3196		3196		
Age (years)	51·7	13·0	50·0	13·3	<0·0001	51·6	13·0	51·6	13·5	0·96
Men (%)	40·5		46·3		<0·0001	40·0		40·4		0·78
BMI (kg/m^2)	22·8	3·2	22·6	3·1	0·003	22·8	3·2	22·8	3·2	0·96
Current smokers (%)	31·5		33·7		0·008	31·4		30·0		0·48
Systolic BP (mmHg)	137·0	21·2	135·2	21·1	<0·0001	137·0	21·2	136·8	21·9	0·68
Diastolic BP (mmHg)	81·8	12·2	81·0	12·1	0·003	81·8	12·2	81·3	12·4	0·11
Hypertension drugs (%)	10·0		6·9		<0·0001	10·0		9·5		0·58
Diabetes (%)	5·4		5·1		0·54	5·4		5·2		0·78
TCH (mg/l)	1880	340	1890	340	0·24	1880	340	1870	330	0·47
Albumin (mg/l)	44	03	44	03	0·66	44	03	44	03	0·91
Uric acid (mg/l)	49	13	50	13	0·07	49	13	50	13	0·76
Creatinine (mg/l)	9·3	1·7	9·4	2·0	0·02	9·3	1·7	9·3	2·1	0·52
Propensity score	0·64	0·05	0·65	0·05	<0·0001	0·64	0·05	0·63	0·05	0·84
(min, max)	0·44	0·80	0·12	0·82		0·44	0·80	0·42	0·76	

BP, blood pressure; TCH, serum total cholesterol concentration.

We merely do not eat foods, but in certain patterns[20], such as those in the Mediterranean and Japanese dietary patterns. Because of highly interrelated dietary exposures, dietary patterns, rather than the specific effects of nutrients or foods, have gained increasing attention[1,2]. Although one drawback of the traditional Japanese diet is a high intake of salt, reduction in salt intake by the Japanese for the last three decades has been considered as one of the chief explanations for the decline in not only stroke but also stomach cancer mortality in Japan[5,6,21,23]. This is consistent with the finding in the present report that infrequent consumption of soups with noodles, a marker of low salt intake, was associated with a significantly lower risk of all-cause mortality by itself.

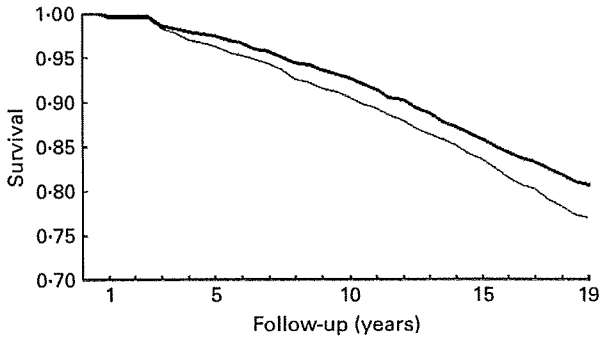

Fig. 1. Kaplan–Meier survival curve after propensity score matching. Significant differences in the average propensity score and the variables used in its calculation before matching in the two groups disappeared after matching. By contrast, a significant difference between the matched survival curves remained as shown in the figure (P=0·0003 by log-rank test). Survival differences by the group were significant when examined further using a regression model with a Weibull distribution that included adjustment for age and sex as the dependent variables (P<0·0001). The thick line indicates survival for the participants with the Reduced-Salt Japanese Diet Score 4–7 and the thin line with the Reduced-Salt Japanese Diet Score 0–3.

Strengths and limitations of the study

The strengths of the present study include its prospective design and the follow-up of a randomly selected sample from the general population of Japan with a high response rate (76 %). Since the study includes both men and women with a broad range of ages, findings are likely to be generalisable to middle-aged and elderly Japanese men and women.

As in any long-term follow-up study, however, there are several weaknesses. First, we surveyed essential nutritional components by the food-frequency method once at the baseline. As a result, we have no data on total caloric intake or total dietary intake of cholesterol or saturated and PUFA. To obtain these data, detailed food records or 24-h recalls are needed. However, these methods are impractical and seldom used as the primary method for estimating usual intake in large-scale epidemiological studies. A second limitation is that the items used for the food-frequency method were not large in number, and has not been validated. We do not have data to what extent these foods contribute to the average energy intake of the studied participants. We also do not have frequency data on tofu, other soya bean products and vegetables and fruits. A high intake of these foods may also be characteristic features of the traditional Japanese diet. Several studies indicate that these foods have beneficial effects on some cause-specific mortality[24,25]. In addition, although the use of near-median values as cut-points for the consumption of meat and tsukemono appears arbitrary, they were chosen in accordance with their use in the previous studies of the Mediterranean diet[2]. Unfortunately, while the intake of tsukemono, infrequent consumption of soup with noodles and occasional drinking appeared to have the strongest association with a reduced risk of mortality, we cannot be certain that the other components of the Japanese diet are less important. As in any observational study, it is difficult to identify specific dietary effects due to multicollinearity that exists among food item intake. Within each component of the Japanese diet, there can also be considerable heterogeneity in nutrient

NS British Journal of Nutrition

content. In addition, overlap between components often occurs with the sharing of common ingredients or in how they are prepared and served. To better identify the effects of specific nutrients on mortality would require a controlled clinical trial. It may also be that dietary factors need to be considered in combination for an effect on longevity to be observed. An additional limitation is that we used mortality data as end points, which may lead to the misclassification of the cause of deaths. However, it has been reported that the death-certificate diagnosis for stroke and cancer in Japan is quite accurate[26]. Possible misclassification of acute myocardial infarction as 'heart failure' is also not an issue in the present report since both outcomes are collectively categorised as CVD[27].

Conclusions

Adherence to a healthy Japanese diet was associated with an approximate 20 % lower rate of all-cause and cardiovascular mortality. While Japanese are exceptionally long lived, placing greater emphasis on the intake of foods that are low in salt could increase longevity in Japan further.

Acknowledgements

The authors thank all members of the Japanese Association of Public Health Center Directors and all staffs of the public health centres who cooperated with the present study. Investigators and members of the research group are listed in the appendix of Nakamura *et al.* [11]. Y. N. participated in designing and conducting the study, analysing and interpreting the data, and writing and preparing the manuscript. H. U. was the principal investigator and participated in designing and conducting the study and analysing and interpreting the data. T. O., R. D. A. and A. O. participated in conducting the study and analysing and interpreting the data. T. K. and Y. K. participated in managing and interpreting the data. T. H. participated in managing the data and conducting the study. We all have no conflicts of interest to disclose. The present study was supported by the Research Grant for Cardiovascular Diseases (7A-2) from the Ministry of Health, Labour and Welfare and a Health and Labour Sciences Research Grant, Japan (Comprehensive Research on Aging and Health: H11-Chouju-046, H14-Chouju-003, H17-Chouju-012), and by the Japan Society for the Promotion of Science Invitation Fellowship Programmes for Research, Japan.

References

1. Huijbregts P, Feskens E, Rasanen L, *et al.* (1997) Dietary pattern and 20 year mortality in elderly men in Finland, Italy, and The Netherlands: longitudinal cohort study. *BMJ* **315**, 13–17.
2. Trichopoulou A, Costacou T, Bamia C, *et al.* (2003) Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med* **348**, 2599–2608.
3. Robertson TL, Kato H, Gordon T, *et al.* (1977) Epidemiologic studies of coronary heart disease and stroke in Japanese men living in Japan, Hawaii and California. Coronary heart disease risk factors in Japan and Hawaii. *Am J Cardiol* **39**, 244–249.
4. Carroll KK (1975) Experimental evidence of dietary factors and hormone-dependent cancers. *Cancer Res* **35**, 3374–3383.
5. Ueshima H, Zhang XH & Choudhury SR (2000) Epidemiology of hypertension in China and Japan. *J Hum Hypertens* **14**, 765–769.
6. Kubo M, Kiyohara Y, Kato I, *et al.* (2003) Trends in the incidence, mortality, and survival rate of cardiovascular disease in a Japanese community: the Hisayama study. *Stroke* **34**, 2349–2354.
7. Nagata C, Takatsuka N, Shimizu N, *et al.* (2004) Sodium intake and risk of death from stroke in Japanese men and women. *Stroke* **35**, 1543–1547.
8. Okamura T, Kadowaki T, Hayakawa T, *et al.* (2003) What cause of mortality can we predict by cholesterol screening in the Japanese general population? *J Intern Med* **253**, 169–180.
9. Nakamura Y, Okamura T, Tamaki S, *et al.* (2004) 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* **80**, 58–63.
10. Nakamura Y, Ueshima H, Okamura T, *et al.* (2005) Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980–99. *Am J Med* **118**, 239–245.
11. Nakamura M, Sato S & Shimamoto T (2003) Improvement in Japanese clinical laboratory measurements of total cholesterol and HDL-cholesterol by the US cholesterol reference method laboratory network. *J Atheroscler Thromb* **10**, 145–153.
12. Kromhout D, Bosschieter EB & de Lezenne Coulander C (1985) The inverse relation between fish consumption and 20-year mortality from coronary heart disease. *N Engl J Med* **312**, 1205–1209.
13. Daviglus ML, Stamler J, Orencia AJ, *et al.* (1997) Fish consumption and the 30-year risk of fatal myocardial infarction. *N Engl J Med* **336**, 1046–1053.
14. Iso H, Kobayashi M, Ishihara J, *et al.* (2006) Intake of fish and *n* 3 fatty acids and risk of coronary heart disease among Japanese: the Japan Public Health Center-based (JPHC) Study Cohort I. *Circulation* **113**, 195–202.
15. Tsugane S, Fahey MT, Sasaki S, *et al.* (1999) Alcohol consumption and all-cause and cancer mortality among middle-aged Japanese men: seven-year follow-up of the JPHC study Cohort I. Japan Public Health Center. *Am J Epidemiol* **150**, 1201–1207.
16. Parsons LS (2001) Reducing bias in a propensity score matched-pair sample using greedy matching techniques. In *Proceedings of the Twenty-sixth Annual SAS® Users Group International Conference*, pp. 214–226. Cary, NC: SAS Institute Inc. www2.sas.com/proceedings/sugi26/p214-26.pdf
17. Jacobs DR Jr, Andersen LF & Blomhoff R (2007) Whole-grain consumption is associated with a reduced risk of noncardiovascular, noncancer death attributed to inflammatory diseases in the Iowa Women's Health Study. *Am J Clin Nutr* **85**, 1606–1614.
18. Ueshima H, Iida M, Shimamoto T, *et al.* (1982) Dietary intake and serum total cholesterol level: their relationship to different lifestyles in several Japanese populations. *Circulation* **66**, 519–526.
19. Ueshima H, Okayama A, Saitoh S, *et al.* (2003) Differences in cardiovascular disease risk factors between Japanese in Japan and Japanese-Americans in Hawaii: the INTERLIPID Study. *J Hum Hypertens* **17**, 631–639.
20. Jacques PF & Tucker KL (2001) Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr* **73**, 1–2.
21. Ueshima H, Tatara K & Asakura S (1987) Declining mortality from ischemic heart disease and changes in coronary risk factors in Japan, 1956–1980. *Am J Epidemiol* **125**, 62–72.

NS British Journal of Nutrition

22. Tokui N, Yoshimura T, Fujino Y, *et al.* (2005) Dietary habits and stomach cancer risk in the JACC Study. *J Epidemiol* **15**, Suppl. 2, S98–S108.
23. Tsugane S, Sasazuki S, Kobayashi M, *et al.* (2004) Salt and salted food intake and subsequent risk of gastric cancer among middle-aged Japanese men and women. *Br J Cancer* **90**, 128–134.
24. Sauvaget C, Nagano J, Allen N, *et al.* (2003) Vegetable and fruit intake and stroke mortality in the Hiroshima/Nagasaki Life Span Study. *Stroke* **34**, 2355–2360.
25. Yamamoto S, Sobue T, Kobayashi M, *et al.* (2003) Soy, isoflavones, and breast cancer risk in Japan. *J Natl Cancer Inst* **95**, 906–913.
26. Ron E, Carter R, Jablon S, *et al.* (1994) Agreement between death certificate and autopsy diagnoses among atomic bomb survivors. *Epidemiology* **5**, 48–56.
27. Saito I, Folsom AR, Aono H, *et al.* (2000) Comparison of fatal coronary heart disease occurrence based on population surveys in Japan and the USA. *Int J Epidemiol* **29**, 837–844.

NS British Journal of Nutrition

Appendix NIPPON DATA80 Dietary Questionnaire

Q1.	Do you eat breakfast daily?	Yes	No
Q2.	Do you daily eat green or yellow vegetables, such as carrot or spinach?	Yes	No
Q3.	Do you daily eat fruits?	Yes	No
Q4.	Do you daily eat salad or fresh vegetables?	Yes	No
Q5.	Do you daily eat meat, fish or egg?	Yes	No
Q6.	Do you daily drink milk?	Yes	No
Q7.	Do you eat soya bean products, such as natto (fermented soya beans) or tofu more than three times per week?	Yes	No
Q8.	Do you eat foods cooked with oil more than once daily?	Yes	No
Q9.	Do you eat seaweed, such as kombu or laver more than three times per week?	Yes	No
Q10.	Do you eat potatoes more than three times per week?	Yes	No

For each food listed on Q11–Q16, please check the box indicating how often you eat, on average

		≥2/d	1/d	1/2 d	1–2/week	<1/week
Q11.	Egg (how many)					
Q12.	Fish (how often)					
Q13.	Meat (including ham and sausage, how often)					
Q14.	Noodles (how often)					
Q15.	Tsukemono (how often)					
Q16.	Soup (including miso soup, how often)					

Q17. Please select one food from the list that you like to eat the most:
(1) Beef (2) Pork (3) Poultry (4) Undecidable

Q18. Please select one dish from the list that you like to eat the most:
(1) Egg food (2) Meat dishes (3) Fish dishes (4) Tofu food (5) A vegetable dish

Q19. Please select one food combination from the list that you like to eat the most:
(1) Rice bowl + sashimi + miso soup + tsukemono
(2) Bread + hamburger steak + potage soup + salad
(3) Rice bowl + hamburger steak + miso soup + salad

Q20. Which type of seasoning do you like best to eat with?
(1) Thick (2) Intermediate (3) Light

Q21. How do you eat tsukemono?
(1) As it is (2) Seasoning with soya sauce (3) Seasoning with sodium glutamate
(4) Seasoning with soya sauce plus sodium glutamate

From Q22 to Q31, please choose one that fits best your recent eating habit

Q22.	Do you try to eat modest amount of food?	Yes	No
Q23.	Do you often eat processed foods, such as ham, sausage, kamaboko or a tubular fish meat?	Yes	No
Q24.	Are you not satisfied if you do not eat with tsukemono?	Yes	No
Q25.	Are you not satisfied if you do not eat with a kind of soup?	Yes	No
Q26.	Do you take soup infrequently with noodles?	Yes	No

Q27.	When you eat tofu served cold, how do you season it with soya sauce? (1) Dip it in a small dish with soya sauce (2) Pour soya sauce over tofu.		
Q28.	When you eat curry and rice, do you pour Worcestershire sauce or soya sauce over it?	Yes	No
Q29.	Are you trying to eat soups less often?	Yes	No
Q30.	Have you ever used low-salt soya sauce?	Yes	No
Q31.	Are you trying to eat tsukudani (a shellfish boiled in sweetened soya sauce), shiokara (fish guts pickled in salt), or salted salmon less often?	Yes	No

NS British Journal of Nutrition

糖尿病男性患者における飲酒と循環器疾患死亡について

研究分担者　中村　保幸　（京都女子大学家政学部生活福祉学科　教授）
研究代表者　上島　弘嗣　（滋賀医科大学生活習慣病予防センター　特任教授）
研究協力者　門田　文　（滋賀医科大学社会医学講座公衆衛生学部門　客員助教）
研究分担者　寶澤　篤　（東北大学大学院医学系研究科社会医学講座公衆衛生学分野　助教）
研究分担者　岡村　智教　（国立循環器病センター予防検診部　部長）
研究協力者　門脇　紗也佳（滋賀医科大学社会医学講座公衆衛生学部門　客員助教）
研究協力者　門脇　崇　（滋賀医科大学社会医学講座公衆衛生学部門　助教）
研究分担者　早川　岳人　（福島県立医科大学衛生学・予防医学講座　准教授）
研究分担者　喜多　義邦　（滋賀医科大学社会医学講座公衆衛生学部門　講師）
研究協力者　Robert D. Abbott（バージニア大学医学部　教授）
研究分担者　岡山　明　（財団法人結核予防会第一健康相談所　所長）

目的

正常者に比べ糖尿病患者では死亡リスクが増加するが、その大部分が心血管疾患による死亡である。わが国においても他の先進諸国と同様、糖尿病の有病率が増加している。糖尿病患者では飲酒を禁止ないし控えるように生活指導されることが多い。その理由として飲酒による摂取カロリーの増加、多量飲酒は糖尿病患者に低血糖が起こっても自覚できなくなる、また飲酒の結果食餌療法が守られなくなるなどが挙げられる。一方近年の欧米での研究結果では総じて適量飲酒は糖尿病患者においても正常者と同様に心血管死亡や総死亡を減少させることを示している。この結果をわが国民に演繹することは危険である。なぜなら欧米と異なりわが国では心血管死亡の中で脳卒中が心筋梗塞より多く、また脳卒中では飲酒により発症・死亡が増加するとの報告があるからである。本研究の目的は中年男性の飲酒習慣と死因別死亡、総死亡との関連を糖尿病の有無について検討することにあった。

方法

1980年に実施された国民栄養調査をもとに19年間の死因追跡を行ったNIPPON DATA80のデータセットを用いた。1980年に無作為抽出した全国300ヵ所において30才以上の男女を対象として検診を行い、食事栄養調査、生活習慣調査と血液生化学検査を行った。1980年の追跡開始時に冠動脈疾患、脳卒中既往がある者は除外した。また女性においては飲酒習慣がある研究参加者が少なかったので、本研究の解析対象は男性のみとした。糖尿病は空腹時血糖126mg/dl以上、随時血糖200mg/dl以上、糖尿病と診断された者の何れかとし、耐糖能異常は空腹時血糖100～126mg/dl、随時血糖140～200 mg/dlと定義した。正常男性が3,614人、耐糖能異常が195人、糖尿病が209人あった。

結果

19年間の追跡期間中に990人が死亡し、うち328人は心血管疾患死亡、157人は全心臓死であった。未飲酒者を基準とし、年齢、BMI、喫煙、血糖値、採血時の食後時間を調整因子として解析すると、耐糖能異常＋糖尿病患者の中で機会飲酒者と毎日飲酒者の心血管死ハザード比（HR）はそれぞれ 0.43(95%信頼区間：0.19-0.95)、0.45(0.25-0.80)であり、全心臓死 HR はそれぞれ 0.33 (0.12-0.91)、0.31(0.15-0.67)であった。

結論

健常人と同様耐糖能異常＋糖尿病患者での飲酒は心血管死と全心臓死のリスクを低下させた。耐糖能異常または糖尿病患者に適量飲酒を禁止する根拠は認められなかった。

ELSEVIER

Alcohol 43 (2009) 635–641

ALCOHOL

Alcohol intake and 19-year mortality in diabetic men: NIPPON DATA80

Yasuyuki Nakamura[a,b,*], Hirotsugu Ueshima[b], Aya Kadota[b], Atsushi Hozawa[b], Tomonori Okamura[b], Sayaka Kadowaki[b], Takashi Kadowaki[b], Takehito Hayakawa[c], Yoshikuni Kita[b], Robert D. Abbott[b,d], Akira Okayama[e]
for NIPPON DATA80 Research Group

[a]*Cardiovascular Epidemiology, Kyoto Women's University, 35 Imakumano Kitahiyoshi-cho, Higashiyama-ku, Kyoto 605-8501, Japan*
[b]*Department of Health Science, Shiga University of Medical Science, Seta Tsukinowa-cho, Otsu City, Shiga 520-2192, Japan*
[c]*Department of Hygiene & Preventive Medicine, Fukushima Medical University, 1 Hikariga-oka, Fukushima City, Fukushima 960-1295, Japan*
[d]*Division of Biostatistics and Epidemiology, University of Virginia School of Medicine, PO Box 800717, Charlottesville, VA 22908-0717, USA*
[e]*Department of Preventive Cardiology, National Cardiovascular Center, 7-1 Fujishiro-dai, Suita, Osaka 565-8565, Japan*

Received 28 August 2008; received in revised form 3 April 2009; accepted 9 June 2009

Abstract

Although moderate alcohol intake in diabetic Caucasians is associated with a reduction in coronary heart disease mortality, no study in Japanese with diabetes has examined the association between alcohol intake and mortality outcomes. We analyzed the relationship between alcohol intake and all-cause and cause-specific mortality using the database from NIPPON DATA80. At the baseline in 1980, data on history, lifestyle, and physical examinations were collected on study participants aged 30 years and older from randomly selected areas in Japan. After excluding participants with comorbidities, we followed 4,018 male participants (3,614 nondiabetics, 195 with impaired glucose tolerance and 209 diabetic) for 19 years. During the 19 years of follow-up, there were 990 deaths; 328 were from cardiovascular disease and 157 from all-heart diseases. With the never-drinking category serving as a reference, the Cox multivariate-adjusted hazard ratios for non-daily and daily drinkers for cardiovascular mortality were 0.43 (95% confidence intervals: 0.19–0.95) and 0.45 (0.25–0.80), respectively, and 0.33 (0.12–0.91) and 0.31 (0.15–0.67) for all-heart disease mortality in the combined impaired glucose tolerance and diabetic Japanese men. Alcohol drinking in men with glucose intolerance was associated with a significant reduction in cardiovascular and all-heart disease mortality as seen in the general population in Japan.

Keywords: Alcohol; Diabetes; Glucose intolerance; Cardiovascular disease; Cohort study

Introduction

An increase in mortality from diabetes mellitus is mostly because of complications from atherosclerotic cardiovascular diseases (Calles-Escandon et al., 1999). Although epidemiological studies have shown an inverse association between moderate alcohol intake and coronary heart disease (CHD) incidence and mortality in general populations (Koppes et al., 2006), alcohol intake in diabetes is often discouraged in today's clinical practice because of concerns that alcohol adds calories without nutritional benefit; excessive alcohol intake by a person who is fasting or skipping meals can lead to hypoglycemia via inhibition of gluconeogenesis, whereas intoxication can impair a person's ability to follow a prescribed management plan or to recognize symptoms of hypoglycemia (Rimm et al., 1999). However, recent studies carried out in North America and Europe confirmed that light to moderate intake of alcohol is associated with a reduction in mortality from CHD and all-cause mortality in patients with diabetes (Ajani et al., 2000; Chalmers, 2005; Diem et al., 2003), and they are consistent with previous results in people without diabetes. However, these results cannot be extrapolated to the Japanese population because the mortality from stroke is higher than that from CHD in Japan, as well as in Korea and China (WHO, 1999), and it is known that alcohol intake differentially affects mortality from these two cardiovascular diseases in Japanese (Iso et al., 2004a; WHO, 1999). Furthermore, a study indicated that moderate to high alcohol consumption was positively associated with the incidence of diabetes in lean (body mass index [BMI] ≤ 22 kg/m^2) Japanese, and among men with a BMI > 22 kg/m^2, a small nonsignificant increase in odds ratio was observed with alcohol consumption

* Corresponding author. Tel./fax: +81-75-531-2162.
E-mail address: nakamury@kyoto-wu.ac.jp (Y. Nakamura).

0741-8329/09/$ – see front matter
doi: 10.1016/j.alcohol.2009.06.005

(Nakamura et al., 2007), whereas other studies in Japanese and Caucasians showed moderate alcohol consumption was associated with a lower risk of diabetes (Okamura et al., 2003; de Vegt et al., 2002; Waki et al., 2005). Thus, the effect of alcohol on mortality from CHD and cardiovascular diseases in Japanese may be different.

In the present study, we analyzed the relationship between alcohol intake and all-cause and cause-specific mortality in men with and without glucose intolerance using the database of the National Integrated Project for Prospective Observation of Non-communicable Diseases and Its Trends in the Aged, 1980 (NIPPON DATA80). The database includes more than 4,600 male participants from randomly selected regions in Japan who were followed for 19 years (Nakamura et al., 2003, 2005).

Materials and methods

Participants

The participants in this cohort were those in the 1980 National Survey on Circulatory Disorders (Nakamura et al., 2005). A total of 10,897 community-based participants (4,795 men and 6,102 women) aged 30 years and older in 300 randomly selected health districts throughout Japan participated in the survey, which consisted of history taking, physical examinations, blood tests, and a self-administered questionnaire on lifestyle. For the present study, we extracted 4,795 male participants because very few women in Japan drank alcohol. Participants were followed to 1999 (NIPPON DATA80, 1980–99). The participation rate of men was 73.5% before exclusion for reasons mentioned in the following.

We reviewed the residence records of all the study participants for vital status. In death cases, the causes were examined. To verify the cause of death, we used the National Vital Statistics records. The underlying cause of death was coded according to the 9th International Classification of Disease for the National Vital Statistics (ICD9) until the end of 1994 and according to the 10th International Classification of Disease from the beginning of 1995. Deaths were confirmed in each district by computer matching of data from the Vital Statistics records using the district, sex, and dates of birth and death as key codes.

Participants were excluded from follow-up because of a past history of coronary disease, stroke, or significant comorbidities, such as renal insufficiency ($N = 215$), missing baseline data ($N = 167$), or loss to follow-up ($N = 395$). The latter group was excluded because of the absence of a permanent address that was required to link to vital statistics records. The final sample comprised 4,018 male participants. There were no significant differences between participants who were lost to follow-up and those who were included in the present study in terms of several risk factors. Therefore, the potential bias regarding the 395 participants lost to follow-up is thought to be negligible. Permission to use the National Vital Statistics records was obtained from the Management and Coordination Agency, Government of Japan. Ethical approval for this study was obtained from the Institutional Review Board of Shiga University of Medical Science for ethical issues (No. 12–18, 2000).

Biochemical and baseline examinations

The baseline surveys were conducted at public health centers. Baseline blood pressure was measured by trained research nurses using a standard mercury sphygmomanometer on the right arm of seated participants after at least 5 min of rest. Hypertension was defined as a systolic blood pressure $\geq$140 mm Hg, a diastolic blood pressure $\geq$90 mm Hg, or when a participant was receiving medication to treat high blood pressure. Height and weight were measured in stocking feet and light clothing. The BMI was calculated as weight (kg) divided by the square of height (m^2).

A lifestyle survey was also carried out using a self-administered questionnaire. Reported information was confirmed by public health nurses through interviews with the study participants regarding food intake, smoking, drinking, and present and past medical histories. With regard to drinking, participants were asked whether they consumed alcohol, and they had to choose one of the following four categories: (1) almost never drink, (2) drink daily, (3) drink occasionally, and (4) stopped drinking, but used to drink.

Casual blood samples were drawn and centrifuged within 60 min of collection and stored at −70°C until analyses. For a few participants ($N = 105$), blood samples were drawn after overnight fasting. Total cholesterol was analyzed in a sequential auto-analyzer (SMA12/60; Technicon, Tarrytown, NY) at a single laboratory (Osaka Medical Center for Health Science and Promotion) (Bittner and McCleary, 1963). Serum concentrations of glucose were measured by the cupric-neocuproline method (Iso et al., 2004b) and the values were converted so that they better corresponded with the more widely used hexokinase method (MacKay and Mensah, 2004). Participants whose casual blood glucose was $\geq$200 mg/dL, or whose fasting blood glucose was $\geq$126 mg/dL, or who had a self-reported history of diabetes were categorized as having "diabetes mellitus." Participants with casual blood glucose concentrations between 140 and $<$200 mg/dL or whose fasting blood glucose concentrations fell between 100 and $<$126 mg/dL were categorized as having "impaired glucose tolerance (IGT)" (MacKay and Mensah, 2004; Thun et al., 1997).

Statistical analysis

SAS version 9.1 for Windows (SAS Institute, Cary, NC) was used throughout the analyses. To examine the

association between alcohol intake and all-cause and cause-specific mortality, age-adjusted and multivariate-adjusted hazard ratios were calculated using a Cox proportional hazards model for the normal and combined IGT plus diabetes groups. For multivariate analyses (Model 1), we adjusted for age, BMI, and cigarette smoking (never and former smokers, current smokers <20 cigarettes/day, current smokers 20–40 cigarettes/day, and current smokers ≥41 cigarettes/day). Model 1 was further adjusted for blood glucose concentration and postprandial hours to rule out the argument that only well-controlled diabetics took alcohol (Model 2). The never-drinking category served as a reference for comparison with the other categories. The secondary analyses were performed in the IGT and diabetes groups separately.

Results

Baseline characteristics according to glucose tolerance category

There were 3,614 participants in the normal, 195 in the IGT and 209 in the diabetic groups. Table 1 shows the baseline characteristics according to glucose tolerance category. Across the categories from normal to diabetic, the prevalence of hypertension, mean age, glucose, and total cholesterol concentration increased.

Baseline characteristics according to alcohol drinking category

Table 2 shows the baseline characteristics according to alcohol drinking category in the normal group and the glucose intolerance group. In the normal groups, those in the former drinking category were older than those in the other drinking strata. In the glucose intolerance group, this was not observed.

The effect of alcohol intake on all-cause and cause-specific mortality according to alcohol intake category in the normal and abnormal glucose tolerance groups

During the 19 years of follow-up, there were 990 deaths. Among these, 328 were from cardiovascular and 662 were because of non-cardiovascular diseases. Among 662 non-cardiovascular deaths, 337 were because of cancer. Among the 328 cardiovascular deaths, 157 were because of all-heart diseases and 155 were attributed to stroke; 95 from cerebral infarction and 37 from cerebral hemorrhage. Among all 157 heart deaths, 65 were because of acute myocardial infarction and 92 to non-acute myocardial infarction, including 61 from heart failure. Table 3 shows the total person years, number of cases, mortality per 1,000 person years, hazard ratios, and 95% confidence intervals for all-cause and cause-specific mortality for each category of alcohol intake after adjustment for age and other risk factors. Here, analyses are limited to the normal glucose tolerance group with the never-drinking category serving as a reference. Non-daily drinking was associated with a significant reduction in all-cause, cardiovascular, all-heart diseases and non-acute myocardial infarction mortality in the age- and multivariate-adjusted models. No significant associations were observed between alcohol intake and stroke mortality. Daily drinking was associated with a significant increase in cancer mortality. Results of Model 2 were not shown in Table 3 because they were not different from those of Model 1.

In the glucose intolerance group, daily drinking was seen in almost half of the participants, and was associated with a significant reduction in cardiovascular and all-heart disease mortality in all the models. Daily drinking was associated with a significant reduction in acute myocardial infarction mortality in Model 2 (Table 4). Non-daily drinking in the glucose intolerance group was associated with a significant reduction in all-cause, all-heart disease and acute myocardial infarction mortality in Model 2. No significant associations were observed between alcohol intake and stroke mortality.

The secondary analyses in the diabetic men yielded similar results. No significant associations between alcohol intake and mortality were observed in the analyses in the IGT group alone, a possible consequence of limited statistical power and lower mortality as compared with those with diabetes.

Discussion

It was interesting to find that the percentage of daily drinkers among participants with glucose intolerance was

Table 1
Baseline characteristics according to glucose tolerance category—NIPPON DATA80 in 1980, men aged 30 years and older

	Normal	IGT	Diabetes
Number (total = 4,018)	3,614	195	209
Age (year)	49.8 ± 13.1	54.3 ± 14.1**	56.9 ± 11.0**
BMI (kg/m^2)	22.5 ± 2.8	22.4 ± 3.2	23.0 ± 3.2*
Current smoker (%)	63.2	64.1	65.5
Current drinker (%)	75.1	69.2	73.2
Hypertension (%)	48.0	62.6**	67.9**
Serum glucose (mg/dL)	95.6 ± 16.2	154.8 ± 21.2**	165.1 ± 88.9**
Serum TCH (mg/dL)	185.2 ± 32.3	188.9 ± 36.6	195.1 ± 35.6**

IGT = impaired glucose tolerance; BMI = body mass index; TCH = total cholesterol concentration. *$P < .05$, **$P < .01$ normal vs. IGT or diabetes.

Table 2
Baseline characteristics according to alcohol drinking category—NIPPON DATA80 in 1980, men aged 30 years and older

	Never	Former	Non-daily	Daily
Normal				
No (total = 3,614)	716	182	980	1,736
Age (year)	52.1 ± 14.1	58.8 ± 14.8**	47.4 ± 12.6**	49.2 ± 12.1**
BMI (kg/m^2)	22.2 ± 3.1	22.1 ± 2.9	22.8 ± 2.9**	22.8 ± 2.6*
Current smoker (%)	56.4	51.1	59.7	69.2**
Hypertension (%)	41.8	53.3	41.5	53.7**
Serum glucose (mg/dL)	97.2 ± 16.6	96.3 ± 17.7	95.3 ± 16.6*	95.0 ± 15.5**
Serum TCH (mg/dL)	184.2 ± 32.9	184.7 ± 33.3	185.7 ± 31.6	185.4 ± 32.3
IGT + DM				
No (total = 404)	85	31	89	199
Age (year)	60.2 ± 13.3	57.4 ± 10.2	51.7 ± 12.3**	55.4 ± 12.3*
BMI (kg/m^2)	22.5 ± 4.0	23.2 ± 3.2	23.2 ± 2.9	22.5 ± 3.1
Current smoker (%)	58.8	64.5	57.3	70.9*
Hypertension (%)	57.7	61.3**	59.6	71.9*
Serum glucose (mg/dL)	161.4 ± 58.7	161.1 ± 57.8	167.2 ± 76.2	156.2 ± 64.9
Serum TCH (mg/dL)	192.5 ± 39.8	200.4 ± 39.4	191.8 ± 38.4	190.7 ± 32.9

BMI = body mass index; DM = diabetes mellitus; IGT = impaired glucose tolerance; TCH = total cholesterol concentration. *$P < .05$; **$P < .01$ never drinker vs. former, non-daily or daily drinker.

similar to that of normal participants (49.3% vs. 48.0%). Despite the fact that alcohol intake in diabetes is often discouraged in current clinical practice, people with glucose intolerance may not comply with these instructions.

Alcohol intake was shown to increase the risk of total strokes in Japanese because of an increase in the risk of hemorrhagic events (WHO, 1999). In Caucasians, however, it was associated with a reduction in the risk of total strokes (MacKay and Mensah, 2004). Furthermore, a study indicated an unfavorable effect of alcohol intake on the incidence of diabetes in Japanese (de Vegt et al., 2002). The other studies in Japanese and Caucasians, however, suggested that alcohol intake reduces the risk of developing type 2 diabetes (Nakamura et al., 2007; Okamura et al., 2003; Waki et al., 2005). Thus, a study of the effect of alcohol intake on cardiovascular mortality among Japanese with diabetes was highly warranted.

Although alcohol may be a surrogate for favorable socioeconomic or lifestyle factors associated with a reduction in coronary risk (Imhof et al., 2001), the anti-inflammatory action and effects of alcohol on lowering low-density lipoprotein cholesterol could contribute to the link between moderate intake and lower cardiovascular mortality (Hart et al., 1999; Imhof et al., 2001). Most of the apparent benefit of alcohol intake on the risk of myocardial infarction has been attributed to an increase in high-density lipoprotein cholesterol (HDL-C) concentrations (De Oliveira et al., 2000; Gaziano et al., 1993). This effect of alcohol may be even more important among diabetics, because low concentrations of HDL-C are a common feature of diabetes.

Strengths and limitations of the study

The strengths of our study include its prospective design and the follow-up of a randomly selected sample from the general population of Japan with a high response rate (73.5%). Because the study includes men with a broad range of ages, findings are likely to be generalizable to middle-aged and elderly Japanese men.

As in any long-term follow-up study, however, there are several weaknesses. First, problems in the self-reporting of drinking may potentially limit the value of the present study, because such a system may underestimate or overestimate true intake, especially in men who actually consume large amounts of alcohol (Bongers et al., 1999). However, it is possible to assume that heavy drinkers in the present population, whether or not under-reported, were scattered in both the non-daily and daily drinking groups. This may have reduced the apparent benefit in both of these groups. Furthermore, self-reporting has been shown to be useful (De Oliveira et al., 2000), and studies using such a system have provided important information (Choudhury et al., 1994; Hines et al., 2001). A second limitation is that we do not have data on the amount of alcohol consumed. Although the beneficial effects of alcohol on mortality were seen in the non-daily drinking category in the normal men, these effects were also seen in the non-daily, as well as in the daily, drinking category in the men with glucose intolerance. It is possible that the men with glucose intolerance might have limited the amount of alcohol intake, because a larger amount of alcohol intake is associated with an increase in cardiovascular disease mortality (Tsugane et al., 1999). A future study using another cohort's data is required. A third limitation is that we used mortality data as end points, which may lead to misclassification of the cause of death. However, it has been reported that the death-certificate diagnosis for stroke in Japan is quite accurate (Ron et al., 1994). It has also been reported that most cases of sudden cardiac death tend to be described on Japanese death certificates as "CHD," "heart failure," or "unknown cause" (Saito et al., 2000). Furthermore,

Table 3
The effect of alcohol intake on all-cause and cause-specific mortality in 3,614 normal men aged 30 years and older—NIPPON DATA80, 1980–99

	Never	Former	Non-daily	Daily
Number at risk (total = 3,614)	716	182	980	1,736
Person years	11,820	2,596	17,324	30,008
All-cause death (total = 821)	199	88	155	379
/1,000 person years	16.8	33.9	8.9	12.6
Age-adjusted HR	1	1.19 (0.93–1.53)	0.74 (0.60–0.91)	0.98 (0.82–1.16)
Model 1	1	1.20 (0.93–1.54)	0.75 (0.61–0.93)	0.97 (0.81–1.15)
CVD death (total = 264)	72	35	38	119
/1,000 person years	6.1	13.5	2.2	4.0
Age-adjusted HR	1	1.20 (0.80–1.80)	0.53 (0.36–0.79)	0.91 (0.68–1.23)
Model 1	1	1.19 (0.80–1.79)	0.53 (0.36–0.80)	0.90 (0.67–1.21)
Non-CVD death (total = 557)	127	53	117	260
/1,000 person years	10.7	20.4	6.8	8.7
Age-adjusted HR	1	1.18 (0.85–1.63)	0.85 (0.66–1.09)	1.02 (0.82–1.26)
Model 1	1	1.18 (0.86–1.64)	0.87 (0.68–1.12)	1.01 (0.82–1.25)
Cancer death (total = 285)	48	18	64	155
/1,000 person years	4.1	6.9	3.7	5.2
Age-adjusted HR	1	1.13 (0.66–1.95)	1.18 (0.81–1.72)	1.54 (1.11–2.14)
Model 1	1	1.14 (0.66–1.97)	1.21 (0.83–1.76)	1.51 (1.09–2.09)
Stroke death (total = 133)	32	14	20	67
/1,000 person years	2.7	5.4	1.2	2.2
Age-adjusted HR	1	1.05 (0.56–1.98)	0.63 (0.36–1.11)	1.17 (0.76–1.78)
Model 1	1	1.05 (0.56–1.98)	0.65 (0.37–1.13)	1.15 (0.75–1.76)
CerInf death (total = 82)	16	11	12	43
/1,000 person years	1.4	4.2	0.7	1.4
Age-adjusted HR	1	1.59 (0.74–3.43)	0.79 (0.37–1.67)	1.58 (0.89–2.83)
Model 1	1	1.59 (0.73–3.43)	0.80 (0.38–1.69)	1.58 (0.89–2.82)
CerHem death (total = 29)	7	1	3	18
/1,000 person years	0.59	0.39	0.17	0.6
Age-adjusted HR	1	0.34 (0.04–2.75)	0.45 (0.12–1.73)	1.45 (0.60–3.51)
Model 1	1	0.34 (0.04–2.74)	0.45 (0.12–1.76)	1.45 (0.06–3.51)
All-heart death (total = 118)	37	19	15	47
/1,000 person years	3.1	7.3	0.9	1.6
Age-adjusted HR	1	1.29 (0.74–2.25)	0.41 (0.22–0.74)	0.70 (0.45–1.07)
Model 1	1	1.29 (0.74–2.25)	0.41 (0.22–0.75)	0.69 (0.45–1.06)
Non-AMI heart (total = 71)	23	13	7	28
/1,000 person years	1.95	5.01	0.4	0.93
Age-adjusted HR	1	1.37 (0.69–2.72)	0.31 (0.13–0.72)	0.68 (0.39–1.19)
Model 1	1	1.37 (0.69–2.72)	0.31 (0.13–0.73)	0.69 (0.40–1.21)
AMI death (total = 47)	14	6	8	19
/1,000 person years	1.2	2.3	0.5	0.6
Age-adjusted HR	1	1.14 (0.44–2.99)	0.56 (0.23–1.33)	0.72 (0.36–1.44)
Model 1	1	1.14 (0.43–2.97)	0.57 (0.24–1.36)	0.69 (0.35–1.39)

CVD = cardiovascular disease; CerInf = cerebral infarction; CerHem = cerebral hemorrhage; AMI = acute myocardial infarction; HR = hazard ratio. Total person years of follow-up, death case number, mortality per 1,000 person years (/1,000 person years), HR, and 95% confidence intervals (95% CIs) are shown. Model 1 = multivariate-adjusted Cox analysis, adjusted for age, body mass index, and smoking (never and ex-, current smokers <20 cigarettes/day, current smokers 20–40 cigarettes/day, and current smokers ≥41 cigarettes/day).

mortality statistics for CHD may have been underestimated up to the end of 1994 using ICD9, because deaths from coronary events may have been miscoded as "heart failure" (Saito et al., 2000). However, the magnitude of the effects of alcohol intake on all-heart disease and acute myocardial infarction mortality in the present study were comparable in the normal men and men with glucose intolerance, suggesting that the findings in the current report are valid. In conclusion, non-daily to daily alcohol intake were associated with a reduction in cardiovascular and all-heart disease mortality in Japanese men with diabetes, as in men without diabetes.

Acknowledgments

This study was supported by a grant in aid of the Ministry of Health and Welfare under the auspices of

Table 4
The effect of alcohol intake on all-cause and cause-specific mortality in 404 men aged 30 years and older with glucose intolerance or diabetes mellitus—NIPPON DATA80, 1980–99

	Never	Former	Non-daily	Daily
Number at risk (total = 404)	85	31	89	199
Person years	1,211	498	1,481	3,140
All-cause death (total = 169)	47	16	22	84
/1,000 person years	38.8	32.1	14.9	26.8
Age-adjusted HR	1	0.91 (0.51–1.60)	0.68 (0.41–1.15)	0.97 (0.68–1.40)
Model 1	1	0.90 (0.51–1.58)	0.69 (0.41–1.17)	0.97 (0.67–1.39)
Model 2	1	1.22 (0.81–1.83)	0.55 (0.37–0.82)	0.93 (0.69–1.25)
CVD death (total = 64)	25	4	10	25
/1,000 person years	20.6	8.0	6.8	8.0
Age-adjusted HR	1	0.44 (0.15–1.27)	0.61 (0.29–1.30)	0.56 (0.32–0.99)
Model 1	1	0.43 (0.15–1.25)	0.62 (0.29–1.33)	0.56 (0.32–0.98)
Model 2	1	0.43 (0.15–1.24)	0.46 (0.21–1.02)	0.49 (0.28–0.86)
Non-CVD death (total = 105)	22	12	12	59
/1,000 person years	18.2	24.1	8.1	18.8
Age-adjusted HR	1	1.42 (0.70–2.88)	0.77 (0.38–1.58)	1.43 (0.87–2.35)
Model 1	1	1.41 (0.70–2.86)	0.78 (0.38–1.61)	1.42 (0.87–2.34)
Model 2	1	1.38 (0.68–2.80)	0.71 (0.34–1.46)	1.34 (0.81–2.21)
Cancer death (total = 52)	10	7	3	32
/1,000 person years	8.3	14.1	2	10.2
Age-adjusted HR	1	1.82 (0.69–4.81)	0.37 (0.10–1.37)	1.57 (0.77–3.23)
Model 1	1	1.83 (0.70–4.84)	0.37 (0.10–1.35)	1.58 (0.77–3.25)
Model 2	1	1.81 (0.69–4.77)	0.36 (0.10–1.35)	1.59 (0.77–3.28)
Stroke death (total = 22)	7	0	4	11
/1,000 person years	5.8	0.0	2.7	3.5
Age-adjusted HR	1	—	1.10 (0.31–3.95)	1.01 (0.38–2.66)
Model 1	1	—	1.22 (0.34–4.46)	1.02 (0.39–2.70)
Model 2	1	—	0.91 (0.23–3.54)	0.88 (0.33–2.35)
CerInf death (total = 13)	5	0	2	6
/1,000 person years	4.1	0	1.4	1.9
Age-adjusted HR	1	—	0.82 (0.15–4.57)	0.80 (0.24–2.72)
Model 1	1	—	1.05 (0.18–6.20)	0.85 (0.24–2.95)
Model 2	1	—	0.53 (0.07–3.91)	0.67 (0.19–2.37)
CerHem death (total = 8)	2	0	1	5
/1,000 person years	1.7	0	0.7	1.6
Age-adjusted HR	1	—	0.89 (0.08–10.3)	1.52 (0.29–8.02)
Model 1	1	—	0.85 (0.07–9.96)	1.51 (0.29–7.96)
Model 2	1	—	0.92 (0.08–11.05)	1.67 (0.31–9.18)
All-heart death (total = 39)	17	3	6	13
/1,000 person years	14.0	6.0	4.1	4.1
Age-adjusted HR	1	0.47 (0.14–1.61)	0.50 (0.19–1.29)	0.41 (0.20–0.85)
Model 1	1	0.47 (0.14–1.61)	0.50 (0.19–1.30)	0.41 (0.20–0.85)
Model 2	1	0.47 (0.14–1.61)	0.36 (0.13–0.99)	0.35 (0.17–0.74)
Non-AMI heart (total = 21)	9	2	4	6
/1,000 person years	7.4	4	2.7	1.9
Age-adjusted HR	1	0.72 (0.15–3.35)	0.90 (0.26–3.11)	0.44 (0.15–1.27)
Model 1	1	0.70 (0.15–3.27)	0.93 (0.27–3.22)	0.44 (0.15–1.26)
Model 2	1	0.70 (0.15–3.30)	0.70 (0.19–2.62)	0.39 (0.13–1.13)
AMI death (total = 18)	8	1	2	7
/1,000 person years	6.6	2.0	1.4	2.2
Age-adjusted HR	1	0.30 (0.04–2.41)	0.25 (0.05–1.22)	0.38 (0.14–1.07)
Model 1	1	0.31 (0.04–2.48)	0.25 (0.05–1.22)	0.39 (0.14–1.11)
Model 2	1	0.30 (0.04–2.44)	0.19 (0.04–0.95)	0.34 (0.12–0.96)

CVD = cardiovascular disease; CerInf = cerebral infarction; CerHem = cerebral hemorrhage; AMI = acute myocardial infarction; HR = hazard ratio. Total person years of follow-up, death case number, mortality per 1,000 person years (/1,000 person years), HR, and 95% confidence intervals (95% CI) are shown. Model 1 = multivariate-adjusted Cox analysis, adjusted for age, body mass index, and smoking (never and ex-, current smokers <20 cigarettes/day, current smokers 20–40 cigarettes/day, and current smokers ≥41 cigarettes/day); Model 2 = Model 1 + glucose, postprandial hours.

Japanese Association for Cerebro-cardiovascular Disease Control, a Research Grant for Cardiovascular Diseases (7A-2) from the Ministry of Health, Labor and a Welfare and Health and Labor Sciences Research Grant, Japan (Comprehensive Research on Aging and Health: H11-Chouju-046, H14-Chouju-003, H17-Chouju-012; Comprehensive Research on Cardiovascular Diseases: H19-Seishu-008), and by the Japan Society for the Promotion of Science invitation fellowship programs for research in Japan. The authors thank all the members of the Japanese Association of Public Health Center Directors and all the staff of the public health centers that cooperated with our study. Investigators and members of the research group are listed in the appendix of Okamura et al., 2003.

References

Ajani, U. A., Gaziano, J. M., Lotufo, P. A., Liu, S., Hennekens, C. H., Buring, J. E., et al. (2000). Alcohol consumption and risk of coronary heart disease by diabetes status. Circulation *102*, 500–505.

Bittner, D., and McCleary, M. (1963). The cupric-phenanthroline chelate in the determination of monosaccharides in whole blood. Am. J. Clin. Pathol. *40*, 423–424.

Bongers, I. M., van de Goor, I. A., Garretsen, H. F., and van Oers, H. A. (1999). Aggregate comparisons of self-reported versus nonself-reported drinking in a general population survey. Subst. Use Misuse *34*, 421–441.

Calles-Escandon, J., Garcia-Rubi, E., Mirza, S., and Mortensen, A. (1999). Type 2 diabetes: one disease, multiple cardiovascular risk factors. Coron. Artery Dis. *10*, 23–30.

Chalmers, K. H. (2005). Medical nutrition therapy. In C. R. Kahn, et al. (Ed.), Joslin's Diabetes Mellitus (14th ed.) (pp. 611–631) Philadelphia: Lippincott Williams & Wilkins.

Choudhury, S. R., Ueshima, H., Kita, Y., Kobayashi, K. M., Okayama, A., Yamakawa, M., et al. (1994). Alcohol intake and serum lipids in a Japanese population. Int. J. Epidemiol. *23*, 940–947.

De Oliveira, E., Silva, E. R., Foster, D., Harper, M. M., Seidman, C. E., Smith, J. D., et al. (2000). Alcohol consumption raises HDL cholesterol levels by increasing the transport rate of apolipoproteins A-I and A-II. Circulation *102*, 2347–2352.

Diem, P., Deplazes, M., Fajfr, R., Bearth, A., Muller, B., Christ, E. R., et al. (2003). Effects of alcohol consumption on mortality in patients with Type 2 diabetes mellitus. Diabetologia *46*, 1581–1585.

Gaziano, J. M., Buring, J. E., Breslow, J. L., Goldhaber, S. Z., Rosner, B., VanDenburgh, M., et al. (1993). Moderate alcohol intake, increased levels of high-density lipoprotein and its subfractions, and decreased risk of myocardial infarction. N. Engl. J. Med. *329*, 1829–1834.

Hart, C. L., Smith, G. D., Hole, D. J., and Hawthorne, V. M. (1999). Alcohol consumption and mortality from all causes, coronary heart disease, and stroke: results from a prospective cohort study of Scottish men with 21 years of follow-up. Br. Med. J. *318*, 1725–1729.

Hines, L. M., Stampfer, M. J., Ma, J., Gaziano, J. M., Ridker, P. M., Hankinson, S. E., et al. (2001). Genetic variation in alcohol dehydrogenase and the beneficial effect of moderate alcohol consumption on myocardial infarction. N. Engl. J. Med. *344*, 549–555.

Imhof, A., Froehlich, M., Brenner, H., Boeing, H., Pepys, M. B., and Koenig, W. (2001). Effect of alcohol consumption on systemic markers of inflammation. Lancet *357*, 763–767.

Iso, H., Baba, S., Mannami, T., Sasaki, S., Okada, K., Konishi, M., et al. (2004a). Alcohol consumption and risk of stroke among middle-aged men: the JPHC Study Cohort I. Stroke *355*, 1124–1129.

Iso, H., Imano, H., Kitamura, A., Sato, S., Naito, Y., Tanigawa, T., et al. (2004b). Type 2 diabetes and risk of non-embolic ischaemic stroke in Japanese men and women. Diabetologia *47*, 2137–2144.

Koppes, L. L., Dekker, J. M., Hendriks, H. F., Bouter, L. M., and Heine, R. J. (2006). Meta-analysis of the relationship between alcohol consumption and coronary heart disease and mortality in type 2 diabetic patients. Diabetologia *49*, 648–652.

MacKay, J., and Mensah, G. (2004). The Atlas of Heart Disease and Stroke. World Health Organization. Available at: http://www.who.int/cardiovascular_diseases/en/cvd_atlas_29_world_data_table.pdf. pp. 84–90. Accessed October 28, 2009.

Nakamura, M., Sato, S., and Shimamoto, T. (2003). Improvement in Japanese clinical laboratory measurements of total cholesterol and HDL-cholesterol by the US cholesterol reference method laboratory network. J. Atheroscler. Thromb. *10*, 145–153.

Nakamura, Y., Kita, Y., Iso, H., Ueshima, H., Okada, K., Konishi, M., et al. (2007). Alcohol consumption, alcohol-induced flushing and incidence of acute myocardial infarction among middle-aged men in Japan-Japan Public Health Center-based prospective study. Atherosclerosis *194*, 512–516.

Nakamura, Y., Ueshima, H., Okamura, T., Kadowaki, T., Hayakawa, T., Kita, Y., et al. (2005). Nippon Data80 Research Group. Association between fish consumption and all-cause and cause-specific mortality in Japan: NIPPON DATA80, 1980–99. Am. J. Med. *118*, 239–245.

Okamura, T., Kadowaki, T., Hayakawa, T., Kita, Y., Okayama, A., and Ueshima, H. (2003). Nippon Data80 Research Group. What cause of mortality can we predict by cholesterol screening in the Japanese general population? J. Intern. Med. *253*, 169–180.

Rimm, E. B., Williams, P., Fosher, K., Criqui, M., and Stampfer, M. J. (1999). Moderate alcohol intake and lower risk of coronary heart disease: meta-analysis of effects on lipids and haemostatic factors. Br. Med. J. *319(7224)*, 1523–1528.

Ron, E., Carter, R., Jablon, S., and Mabuchi, K. (1994). Agreement between death certificate and autopsy diagnoses among atomic bomb survivors. Epidemiology *5*, 48–56.

Saito, I., Folsom, A. R., Aono, H., Ozawa, H., Ikebe, T., and Yamashita, T. (2000). Comparison of fatal coronary heart disease occurrence based on population surveys in Japan and the USA. Int. J. Epidemiol. *29*, 837–844.

Thun, M. J., Peto, R., Lopez, A. D., Monaco, J. H., Henley, S. J., Heath, C. W. Jr., et al. (1997). Alcohol consumption and mortality among middle-aged and elderly U.S. adults. N. Engl. J. Med. *337*, 1705–1714.

Tsugane, S., Fahey, M. T., Sasaki, S., and Baba, S. (1999). Alcohol consumption and all-cause and cancer mortality among middle-aged Japanese men: seven-year follow-up of the JPHC study Cohort I. Japan Public Health Center. Am. J. Epidemiol. *150*, 1201–1207.

de Vegt, F., Dekker, J. M., Groeneveld, W. J., Nijpels, G., Stehouwer, C. D., Bouter, L. M., et al. (2002). Moderate alcohol consumption is associated with lower risk for incident diabetes and mortality: the Hoorn Study. Diabetes Res. Clin. Pract. *57*, 53–60.

Waki, K., Noda, M., Sasaki, S., Matsumura, Y., Takahashi, Y., and Isogawa, A., JPHC Study Group (2005). Alcohol consumption and other risk factors for self-reported diabetes among middle-aged Japanese: a population-based prospective study in the JPHC study cohort I. Diabet. Med. *22*, 323–331.

WHO Consultation Group (1999). Part 1: Diagnosis and classification of diabetes mellitus WHO/NCD/NCS/99. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications, 2nd ed., Geneva: World Health Organisation. pp. 1–59.