Meat consumption in relation to mortality from cardiovascular disease among Japanese men and women

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Abbreviations used: JACC Study, The Japan Collaborative Cohort Study; FFQ, food frequency questionnaire; HR, hazard ratio; CI, confidence interval; BCAA, branched-chain amino acid.

Abstract

Background/Objectives: Although high or low (no) meat consumption was associated with elevated or reduced mortality from cardiovascular disease, respectively, few studies have investigated the association between moderate meat consumption and cardiovascular disease. We aimed to evaluate the associations between moderate meat consumption and cardiovascular disease mortality.

Subjects/Methods: We conducted a prospective cohort study of 51 683 Japanese (20 466 men and 31 217 women) aged 40–79 years living in all of Japan (The Japan Collaborative Cohort Study; JACC Study). Consumptions of meat (beef, pork, poultry, liver, and processed meat) were assessed via a food frequency questionnaire administrated at baseline survey. Hazard ratios (HRs) of mortality from cardiovascular disease were estimated from Cox proportional hazards regression models according to quintiles of meat consumption after adjustment for potential confounding variables.

Results: During 820 076 person-years of follow-up, we documented 2 685 deaths due to total cardiovascular disease including 537 ischemic heart diseases and 1 209 strokes. The multivariable HRs (95% CI) for the highest versus lowest quintiles of meat consumption (77.6 versus 10.4 g/day) among men were 0.66 (0.45–0.97) for ischemic heart disease, 1.10 (0.84–1.43) for stroke, and 1.00 (0.84–1.20) for total cardiovascular disease. The corresponding HRs (59.9 versus 7.5 g/day) among women were 1.22 (0.81–1.83), 0.91

(0.70–1.19) and 1.07 (0.90–1.28). The associations were similar when the consumptions of red meat, poultry, processed meat, and liver were examined separately.

Conclusion: Moderate meat consumption, up to approximately 100 g/day was not associated with increased mortality from ischemic heart disease, stroke or total cardiovascular disease among either gender.

Key words: meat, cardiovascular diseases, ischemic heart disease, stroke, mortality, prospective study

Introduction

Meat is a major protein source for humans (ref. 1). Unlike fish or beans, however, meat in particular red or processed meat, is often considered to be unhealthy because of the fact that it is a major source of saturated fatty acid (a reported risk factor for ischemic heart disease in Western countries) (ref. 2–4). Several cohort studies have reported an association between high consumption of meat (which is two to three more times likely in Westerners but not in Japanese) in particular red or processed meat and risk of ischemic heart disease (ref. 5–7) and stroke (ref. 8,9), while one Japanese study showed no association between meat consumption and stroke mortality (ref. 10). The evidence on low (no) meat consumption and cardiovascular disease came from studies of vegetarians (ref. 11–15), although their diet and lifestyles may differ in many ways to that of non-vegetarians. Studies of non-vegetarians or general populations are necessary to evaluate an effect of low to moderate meat consumption on cardiovascular disease, but no studies have examined this issue. In recent decades, the average meat consumption among Japanese increased gradually during the 1990s, and stabilized thereafter (64.2 g/day for total meat in 1975, 82.3 g/day in 1995, 82.6 g/day in 2007) (ref. 1). However, meat consumption among Japanese remains much lower than that among people from Western countries (179.3 g/day for total meat) (ref. 16).

In this paper, we examined the association between moderate meat consumption and mortality from cardiovascular disease in a large prospective study of Japanese men and women.

Subjects and methods

Study Cohort

The Japan Collaborative Cohort (JACC) Study is a population-based study of 110 792 persons (46 465 men and 64 327 women) aged 40–79 during the baseline period (1988–1990), enrolled from 45 communities across Japan. The sampling and protocols of the JACC Study have been described previously (ref. 17). Participants replied to self-administered questionnaires about their lifestyles and medical histories such as cardiovascular disease and cancer (ref. 18). We excluded persons who had a history of heart disease, stroke, or cancer at the baseline survey (n = 5 864), or participants with a missing response to more than four items on the food frequency questionnaire (FFQ; described below) (ref. 19) (n = 46 198). Furthermore, participants with one or more item missing amongst five meat items listed on the dietary questionnaire were excluded (n = 7 047). In addition, we obtained the data of serum total cholesterol levels at municipal health screening examinations from the subsamples of 5 800 men and 11 291 women.

As a result, we included 20 466 men and 31 217 women who provided complete information regarding their dietary information. Written or explicitly verbal informed consent was obtained before their questionnaires were completed. In several communities, informed consent was obtained from community leaders on behalf of the individual participants (a common practice for informed consent in Japan at that time). The JACC Study protocol was approved by the Medical Ethical Committees of the Nagoya University School of Medicine, University of Tsukuba and Osaka University.

Mortality surveillance

In each community, investigators conducted a systematic review of death certificates. In Japan, the registration of residence and death is a legal requirement, so it is assumed that this practice is upheld. The participants moved out from their original community were treated as censored cases, for whom the dates of moving out were obtained from the registration database. Follow-up was conducted through to the end of 2008, except for four communities in which the follow-up had ended in 1999, and another four communities for which it had ended in 2003. The median follow-up period was 18.4 years. We used the underlying cause of death coded by the International Statistical Classification of Diseases and Related Health Problems – 10th Revision (ICD-10) to identify mortality end points: I20–I25 for ischemic heart disease, I60–I69 for stroke, and I01–I99 for total cardiovascular disease.

Consumption of meat

Dietary assessment was evaluated by the FFQ. The FFQ included 33 foods, including 5 meat items: beef, pork, poultry, liver, and processed meat. Liver item was regarded as meat in this study because its in protein and fat contents are similar to lean meat. Five choices were presented for each item with regards to consumption habits: rarely, 1–2 days a month, 1–2 days a week, 3–4 days a week, and almost daily. The portion size per day was estimated by a validation study for FFQ among eighty-five participants. We assigned portion size as 36 g for beef, 41 g for pork, 43 g for poultry, 22 g for processed meat and 53 g for liver (ref. 19). In addition, we multiplied the portion size by 1.3 for men for the following two reasons. First, the portion size estimated from the validation study was primarily for women, because the majority of participants (77 out of 85) in the validation study were women. Second, average meat consumption was 1.3-times higher among men than women according to the National Nutrition Survey in 1990 (ref. 20). We calculated consumption of meat (g/day) from average daily frequencies and portion sizes. Based on the Japan Food Table (Fifth Revised and Enlarged Edition), we calculated the intake of total energy from frequency and portion size of each food (ref. 19).

The reproducibility of this FFQ was confirmed by comparing two questionnaires administered one year apart in the validation study (ref. 19). The Spearman correlation coefficients were 0.59 for beef, 0.44 for pork, 0.53 for poultry, 0.67 for processed meat, and 0.71 for liver. Further, the validity of dietary data was confirmed by comparing the data from the questionnaire with those from four 3-day dietary records, collected approximately three to four months apart (ref. 19). The Spearman correlation coefficients were 0.49 for beef, 0.37 for pork, 0.44 for poultry, 0.63 for processed meat, and 0.20 for liver. The sex-specific mean values (standard deviations) of total meat consumption were 75.9 g (37.1) among men and 55.8 g (24.7) among women for dietary record, and 37.8 g (26.6) among men and 29.8 g (20.8) among women for FFQ.

Statistical analysis

Age-adjusted means and proportions of selected cardiovascular risk factors and foods were calculated according to quintiles of consumptions of total meat, red meat (beef and pork), poultry, processed meat, and liver. Foods were adjusted for energy by the residual method (ref. 21). For each participant, we calculated the person-years of follow-up from baseline to the first end point: death, moving from the community, or the end of 2008. The mortality rates of each outcome were calculated according to quintiles of meat consumption. Gender specific hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated after adjustments for age, and other potential confounding factors using Cox proportional hazards regression models. The statistical testing for linear trends across quintiles of meat consumption was performed by using a median value of each quintile. The confounding factors included body mass index (BMI; gender-specific quintiles), history of hypertension and diabetes mellitus (yes or no), smoking status (never, former, current smoker of 1–19 or ≥20 cigarettes/day) (ref.

22), alcohol intake (never, former drinker, and current drinker of ethanol at 1–22, 23–45, 46–68, or ≥69 g/day), perceived mental stress (low, medium, or high) (ref. 23), walking time (rarely, 30, 30–60, or more than 60 min/day) (ref. 24), sports participation time (rarely, 1–2, 3–4, or more than 5 h/week) (ref. 24), education levels (age of completed education of <13, 13–15, 16–18, or≥19 ye ars), total energy (gender-specific quintiles) and energy-adjusted food (rice, fish, soy, vegetable and fruit) intake (gender-specific quintiles). The self-reported weight and height figures were obtained from the baseline questionnaire. We analyzed this data using SAS version 9.1.3 Service Pack 4 (SAS Institute, Cary, North Carolina). All probability values for statistical tests were two-tailed, and values of $p<0.05$ were regarded as statistically significant.

Results

During 820 076 person-years of follow-up for 51 683 persons (20 466 in men and 31 217 in women), we documented 537 deaths (301 in men and 236 in women) due to ischemic heart disease, 1 209 (589 in men and 620 in women) due to stroke and 2 685 (1 317 in men and 1 368 in women) total cardiovascular deaths.

At baseline, median consumption of total meat was 33.7 g/day for men and 27.0 g/day for women. According to quintiles of energy-adjusted total meat consumption, history of diabetes mellitus was positively associated with total meat consumption. BMI, ethanol intake, blood pressure, history of hypertension were inversely associated with total meat consumption **(Table 1)**. Similar trends were observed according to quintiles of red meat consumption and quintiles of poultry, processed meat, and liver consumptions (not shown in table). In the subsample of 5 800 men and 11 291 women, meat consumption was not associated with serum total cholesterol levels. For men, there were no associations between total meat consumption and age-adjusted mortality from stroke or total cardiovascular disease, though there was an inverse trend with mortality from ischemic heart disease (**Table 2**). After adjustment for cardiovascular risk factors and selected food intakes, the inverse association with mortality from ischemic heart disease remained statistically significant. The multivariable HRs (95% CI) of mortality from ischemic heart disease for the highest versus lowest quintiles of total meat consumption was 0.66 [(0.45–0.97); *P*-trend = 0.015]. For women, total meat consumption was not associated with mortality from ischemic heart disease or total cardiovascular disease in either age-adjusted or multivariable models. Although there was an inverse trend with mortality from stroke in age-adjusted model, the association was no longer statistically significant in multivariable model (Table 2).

The inverse association with ischemic heart disease was similarly observed for red and processed meat consumption among men, whilst no association for any subtype of meat consumption among women (**Table 3**).

Stratified by BMI (< and ≥25 kg/m^2), these associations did not alter except for overweight women (**Table 4**). Among overweight women in which mean BMI was 27.1 kg/m^2, the multivariable HR (95% CI) of mortality from ischemic heart disease for highest versus lowest quintiles of total meat consumption was 2.04 [(0.98–4.26); *P*-trend = 0.040]. The associations between total meat consumption and mortality from stroke or total cardiovascular disease did not vary according to the BMI subgroup among men and women.

The inverse association with ischemic heart disease was not observed for any meat subtype among overweight men, though it was observed for processed meat among non-overweight men (**Supplemental Table 1**). For women, the positive trend was observed for liver consumption among the overweighted, while no association for any meat subtype was shown among the non-overweighted women (**Supplemental Table 2**).

To examine a potential reverse causation for meat consumption and mortality from cardiovascular disease, we analyzed the data by excluding early deaths. When deaths occurring 1–8 years from the baseline (the middle of the follow-up period) were excluded, the associations between total meat consumption and mortality from ischemic heart disease did not change substantially. For example, after the exclusion of deaths within 8 years from the baseline, the multivariable HRs (95% CI) of ischemic heart disease mortality for highest versus lowest quintiles of total meat consumption were 0.69 [(0.44–1.09); *P*-trend = 0.058], among men, and 1.19 [(0.75–1.90); *P*-trend = 0.57], among women. The associations between red meat, processed meat, poultry, or liver with mortality from ischemic heart disease did not change by excluding early deaths.

Discussion

In this large, community-based prospective cohort study, we observed that consumption of total meat was not associated with increased risk of mortality from stroke and total cardiovascular disease. Persons with higher meat consumptions comparing to those with the lowest consumption of total meat, red meat and processed meat were associated with lower risk of mortality from ischemic heart disease for men, while no associations were found for women. Among overweight women (BMI ≥25 kg/m^2), however the highest quintile of meat consumption tended to be associated with the elevated risk.

Japanese meat consumption increased from 64.2 g/day in 1975 to 82.3 g/day in 1995, stabilizing at 82.6 g/day in 2007 (ref. 1). Age-adjusted mortality rates from ischemic heart disease declined from 46.3 per 100 000 in 1990 to 38.7 per 100 000 in 2007 for men and from 25.6 per 100 000 to 17.0 per 100,000 for women (ref. 25). This paradoxical trend in mortality from ischemic heart disease was probably due to the improvement of other risk factors, such as a substantial reduction of blood pressure levels for both men and women, and a decline in the proportion of male smoking. In the present study, meat consumption was inversely associated with blood pressure levels and smoking, suggesting that Japanese with a moderate meat consumption had a beneficial profile of these cardiovascular risk factors.

The meta-analysis of 20 studies (1 218 380 individuals at risk and 23 889 coronary heart diseases) showed that processed meat, but not red meat was associated with higher risk of coronary heart disease (ref. 26). The overall relative risks (95% CI) for coronary heart disease were 1.42 (1.07–1.89) per 50 g serving of processed meat per day and 1.00 (0.81–1.23) per 100 g serving of red meat per day (ref. 26). However, as far as moderate meat consumption (up to 100 g/day) previous studies of Americans and Europeans revealed no excess risks of stroke (ref. 8,9), ischemic heart disease (ref. 27) and total cardiovascular disease (ref. 5).

We observed the potential excess risk of ischemic heart disease associated with meat consumption among overweight women (mean BMI = 27.2 kg/m^2). Our finding is constant with a cohort study of Americans women (BMI = 26 kg/m^2) which showed a significant association between meat consumption and risk of ischemic heart disease (ref. 27).

We excluded deaths that occurred within 1 to 8 years from the baseline in order to reduce the potential bias of preexisting illness and disease (such as dyslipidemia, diabetes mellitus, and hypertension) which may have lowered individual’s meat consumptions due to a belief that meat may be harmful to their health. However, after the exclusion of early deaths within 8 years of the baseline, the association did not change substantially, suggesting that the reverse causation is unlikely.

Several mechanisms were considered about adverse effects of meat consumption, because of high amount of haem iron, saturated fat and for processed meat, sodium. Haem iron increases risks of carotid atherosclerosis and type 2 diabetes probably through the form action of hydroxyl radicals (ref. 28,29). That oxidative stress induces insulin resistance through inhibition of normal phosphorylation of insulin receptor substrate proteins, and reduction of bioavailability of nitric oxide as a regulator of endothelial function through the peroxynitrite formation (ref. 30). High sodium intake increases blood pressure levels (ref. 31,32). High intake of saturated fat rich in meat increases total and low-density lipoprotein (LDL) cholesterol levels (ref. 33). Taken together, all of these effects may contribute to increase risk of ischemic heart disease. However, in the present study, total meat consumption was not associated with serum total cholesterol levels. Therefore, the positive association between total meat consumption and mortality from ischemic heart disease among the overweighted women was not explained by serum total cholesterol.

Additionally, the mechanisms for the no positive association which observed between meat consumption and cardiovascular disease mortality observed in the present study are uncertain, but a potential effect of amino acids can be considered. Several amino acids such as branched-chain amino acids (BCAAs), L-arginine, tryptophan and tyrosine are richer in animal foods but poor in rice. BCAAs promote the anabolic effect of cardiac protein which may protect heart from ischemic damage (ref. 34). L-arginine, a substrate for nitric oxide, produces an immediate reduction in systolic and diastolic blood pressures in humans (ref. 35). Tryptophan and tyrosine have an antihypertensive effect in rats due to serotonin formation in the central nervous system (ref. 36,37). However, we need further investigations whether these bioactivities affect risk of cardiovascular disease through moderate meat consumption.

The strengths of our study include its large cohort size, which provided us with strong statistical power, and a single study with a standardized protocol. The Japanese population's mean levels of total meat consumption were approximately half to one third of those of Western people (ref. 16). Traditional Japanese diet consists rice, miso soup, and three dishes. One of the dishes is meat or fish, and the other two dishes are usually vegetables. In addition, the common cooking way of meat is boiling or stir-frying with vegetables rather than grilling like barbecue, the portion size of meat is generally small. Therefore, our study could effectively examine the relationship between moderate meat consumption and mortality from cardiovascular disease.

There were also several limitations in the present study. First, for people who selected the highest category of meat consumption frequency (namely, almost daily), we could not estimate how many times they ate meat daily. This may have led to the underestimation of meat consumption. The estimated median meat consumption in the present study (33.7 g/day for men and 27.0 g/day for women) was less than half that estimated from dietary records in the validation study (75.9 g/day among men and 55.8 g/day among women) (ref. 19). Although the amount of meat consumed could be underestimated, the ranking of meat consumption was unlikely to change in this study. Second, a number of participants were excluded because they did not respond sufficiently to the FFQ. The non-respondents were older (58.8 years compared to 55.9 years), highly educated (high school or lower education achieved: 6% compared to 13%) and male (44% versus 40%), compared with respondents, though there were small differences in other baseline characteristics. Thus, a potential selection bias may be small. Lastly, we cannot negate the possibility of residual confounding by other unexamined life-styles or socioeconomic status.

In conclusion, moderate meat consumption, up to approximately 100 g/day was not associated with increased mortality from ischemic heart disease, stroke, or total cardiovascular disease among Japanese men and women. The potential excess risk of ischemic heart disease associated with meat consumption among overweight women needs further investigation.

Supplementary information is available at European Journal of Clinical Nutrition's website.

Conflict of interest

The authors declare no conflict of interest.

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Table 1.

Sex-specific age-adjusted mean values or prevalence of cardiovascular risk factors according to quintiles of total meat consumption.[1]

	Men					*P* for	Women					*P* for
Quintile of total meat consumption[2]	Q1(low)	Q2	Q3	Q4	Q5(high)	trend[3]	Q1(low)	Q2	Q3	Q4	Q5(high)	trend[3]
Men												
Meat consumption, *median* (g/day)	10.4	23.1	33.9	46.6	77.6		7.5	18.7	27.1	37.1	59.9	
Range (g/day)	(0.7-17.4)	(17.4-28.7)	(28.7-39.5)	(39.5-55.2)	(55.2-277.1)		(0.4-13.9)	(13.9-23.1)	(23.1-31.5)	(31.5-43.7)	(43.7-221.6)	
Meat consumption (times/day)	0.21	0.49	0.71	0.95	1.52		0.20	0.53	0.74	1.00	1.50	
Participants at risk (n)	4093	4093	4094	4093	4093		6243	6244	6243	6244	6243	
Age (years)	56.6	55.7	55.3	55.0	55.8	0.006	58.8	56.7	55.5	55.0	54.3	<0.001
BMI (kg/m^2)	22.8	22.8	22.7	22.6	22.5	<0.001	23.0	22.9	22.9	22.8	22.8	<0.001
Smoker (%)	56.5	54.0	53.4	52.2	54.5	0.078	6.1	4.6	4.3	4.2	4.7	0.003
Ethanol intake (g/day)	37.1	35.4	34.1	32.8	31.0	<0.001	12.8	11.6	9.6	9.0	8.0	<0.001
Walking time 30min or more /day (%)	67.4	70.3	70.3	69.2	68.7	0.720	70.6	73.0	73.2	73.2	71.2	0.850
Sports time 1h or more /week (%)	27.5	31.9	32.6	33.1	32.4	<0.001	19.6	22.1	25.0	24.8	24.8	<0.001
Sleep duration (h/day)	7.4	7.4	7.4	7.4	7.4	0.020	7.1	7.1	7.1	7.1	7.0	0.046
College or higher education (%)	18.2	18.1	19.2	18.0	19.3	0.256	8.5	9.6	11.5	11.1	11.5	<0.001
High perceived mental stress (%)	25.0	24.5	23.4	24.7	26.7	0.033	20.7	20.5	20.7	20.8	20.9	0.597
History of hypertension (%)	18.8	18.5	17.2	17.0	16.1	<0.001	20.2	19.7	18.8	18.4	17.6	<0.001
History of diabetes (%)	5.3	5.5	5.6	5.9	5.9	0.177	3.1	3.1	2.7	3.2	3.6	0.083
Menopause (%)							62.6	65.4	64.3	63.1	61.2	<0.001
Rice intake (g/day)[4]	571.1	539.6	515.1	490.6	441.5	<0.001	467.8	433.8	415.0	389.7	352.5	<0.001
Fish and fish products intake (g/day)[4]	44.4	46.4	48.8	51.0	57.4	<0.001	48.4	48.0	48.7	50.5	54.2	<0.001
Vegetables intake (g/day)[4]	80.3	88.2	93.5	98.9	110.0	<0.001	101.3	102.7	105.5	110.1	117.5	<0.001
Fruits intake (g/day)[4]	107.5	116.3	123.7	125.2	135.7	<0.001	142.4	146.9	149.8	153.8	155.0	<0.001
Energy intake (kcal/day)	1731	1811	1795	1766	1722	<0.001	1395	1487	1452	1430	1367	<0.001
Systolic blood pressure (mmHg)[5]	134.7	133.5	133.5	133.0	132.3	<0.001	131.1	130.4	130.0	130.1	129.7	<0.001
Diastolic blood pressure (mmHg)[5]	81.0	80.0	80.1	80.1	79.3	<0.001	77.0	77.0	76.9	77.0	76.8	0.211
Subsamples with serum chemistry (n)	1133	1226	1186	1126	1129		2092	2181	2285	2283	2450	
Total cholesterol (mmol/l)	4.90	4.90	4.94	4.87	4.92	0.837	5.27	5.30	5.28	5.27	5.25	0.200

[1] Meat consumption was estimated as the frequency scores and portion size of 5 meat items (beef, pork, poultry, liver, and processed meat).

[2] Energy adjusted quintiles by residual method.

[3] Based on tests for trend across quintiles of meat intake by assigning the median value of each quintile.

[4] Food intakes were adjusted for total energy intake by the residual method.

[5] Systolic blood pressure and diastolic blood pressure were obteined at baseline survey by self reported.

Table 2.

Sex-specific hazard ratios (HR) and 95% confidence intervals (95% CI) of mortality from ischemic heart disease, stroke and total cardiovascular disease according to quintiles of total meat consumption (energy adjsuted).

	Quintile of total meat consumption									
	Q1(low)	Q2		Q3		Q4		Q5(high)		*P* for
	reference	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	trend[1]
Men (n)	4093	4093		4094		4093		4093		
Person-Years	62660	64307		64761		64405		62954		
Ischemic heart disease (n)	74	65		63		49		50		
Age-adjusted HR	1.00	0.90	(0.65-1.26)	0.89	(0.63-1.24)	0.72	(0.50-1.03)	0.70	(0.49-1.01)	0.027
Multivariable HR[2]	1.00	0.97	(0.69-1.36)	0.92	(0.65-1.30)	0.73	(0.50-1.06)	0.66	(0.45-0.97)	0.015
Total stroke (n)	130	105		122		101		131		
Age-adjusted HR	1.00	0.85	(0.66-1.10)	1.00	(0.78-1.28)	0.86	(0.66-1.11)	1.05	(0.82-1.33)	0.560
Multivariable HR[2]	1.00	0.91	(0.70-1.19)	1.08	(0.83-1.39)	0.92	(0.70-1.20)	1.10	(0.84-1.43)	0.461
Total cardiovascular disease (n)	300	260		246		233		278		
Age-adjusted HR	1.00	0.91	(0.77-1.07)	0.87	(0.74-1.03)	0.86	(0.72-1.01)	0.96	(0.82-1.14)	0.721
Multivariable HR[2]	1.00	0.98	(0.83-1.16)	0.94	(0.79-1.12)	0.93	(0.78-1.11)	1.00	(0.84-1.20)	0.988
Women (n)	6243	6244		6243		6244		6243		
Person-Years	98857	100192		100918		100589		100433		
Ischemic heart disease (n)	73	44		39		35		45		
Age-adjusted HR	1.00	0.80	(0.55-1.17)	0.79	(0.54-1.17)	0.73	(0.49-1.10)	1.00	(0.69-1.46)	0.851
Multivariable HR[2]	1.00	0.89	(0.60-1.30)	0.93	(0.62-1.40)	0.89	(0.58-1.35)	1.22	(0.81-1.83)	0.397
Total stroke (n)	185	138		100		103		94		
Age-adjusted HR	1.00	0.97	(0.78-1.21)	0.78	(0.61-1.00)	0.83	(0.65-1.06)	0.81	(0.63-1.04)	0.041
Multivariable HR[2]	1.00	1.02	(0.82-1.28)	0.88	(0.68-1.13)	0.92	(0.72-1.19)	0.91	(0.70-1.19)	0.357
Total cardiovascular disease (n)	407	265		233		232		231		
Age-adjusted HR	1.00	0.86	(0.74-1.01)	0.84	(0.72-0.99)	0.87	(0.74-1.02)	0.92	(0.78-1.08)	0.288
Multivariable HR[2]	1.00	0.91	(0.77-1.06)	0.93	(0.79-1.10)	0.98	(0.83-1.16)	1.07	(0.90-1.28)	0.351

[1] Based on tests for trend across quintiles of meat consumption by assigning the median value of each quintile.

[2] Cox proportional hazard models adjusted for age, BMI, ethanol intake, perceived mental stress, walking time, sports participation time, education years, history of hypertension and diabetes, total energy, and energy adjusted food (rice, fish, soy, vegetables and fruits) intakes.

Table 3.

Sex-specific multivariable hazard ratios (HR) and 95% confidence intervals (95% CI) of mortality from ischemic heart disease according to quintiles of each meat consumptions (energy adjsuted).

	Quintile of each meat consumptions									
	Q1(low)	Q2		Q3		Q4		Q5(high)		*P* for
	reference	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	trend[1]
Men (n)	4093	4093		4094		4093		4093		
Red meat										
Median intake (g/day)	6.4	15.5		23.3		33.2		57.8		
Person-Years	62785	64247		64694		64366		62995		
No. of cases	69	74		53		59		46		
Multivariable HR[2]	1.00	1.19	(0.85-1.65)	0.88	(0.61-1.27)	1.00	(0.70-1.44)	0.7	(0.47-1.04)	0.038
Poultry										
Median intake (g/day)	1.9	3.3		10.2		13.3		27.3		
Person-Years	63758	62452		65983		64031		62863		
No. of cases	67	68		51		49		66		
Multivariable HR[2]	1.00	0.85	(0.58-1.25)	0.93	(0.63-1.37)	0.63	(0.41-0.96)	0.86	(0.60-1.23)	0.405
Processed meat										
Median intake (g/day)	1.2	1.5		2.9		6.1		13.9		
Person-Years	64599	62210		61509		66035		64734		
No. of cases	62	72		74		50		43		
Multivariable HR[2]	1.00	1.01	(0.66-1.54)	0.87	(0.55-1.37)	0.80	(0.53-1.21)	0.56	(0.36-0.88)	0.002
Liver										
Median intake (g/day)	1.2	1.5		2.7		3.6		15.2		
Person-Years	66472	62899		64653		63822		61240		
No. of cases	56	74		63		42		66		
Multivariable HR[2]	1.00	0.95	(0.61-1.48)	1.02	(0.69-1.51)	0.72	(0.46-1.15)	0.95	(0.63-1.42)	0.838
Women (n)	6243	6244		6243		6244		6243		
Red meat										
Median intake (g/day)	4.0	11.5		17.8		25.5		43.9		
Person-Years	98901	100792		101160		100591		99544		
No. of cases	77	47		30		38		44		
Multivariable HR[2]	1.00	0.96	(0.66-1.40)	0.71	(0.46-1.10)	1.02	(0.68-1.54)	1.23	(0.82-1.85)	0.317
Poultry										
Median intake (g/day)	1.5	4.2		8.6		11.3		22.4		
Person-Years	99439	98542		102799		99074		101134		
No. of cases	48	55		40		50		43		
Multivariable HR[2]	1.00	1.09	(0.72-1.66)	1.24	(0.78-1.98)	1.12	(0.72-1.74)	1.06	(0.69-1.62)	0.888
Processed meat										
Median intake (g/day)	0.9	1.2		2.2		4.7		10.4		
Person-Years	100156	97701		97896		103346		101890		
No. of cases	44	60		63		32		37		
Multivariable HR[2]	1.00	1.12	(0.68-1.84)	1.04	(0.61-1.84)	0.92	(0.56-1.50)	0.98	(0.59-1.62)	0.631
Liver										
Median intake (g/day)	0.9	1.0		1.6		2.3		11.1		
Person-Years	103829	100394		98706		100520		97540		
No. of cases	42	54		55		31		54		
Multivariable HR[2]	1.00	0.91	(0.50-1.67)	0.66	(0.37-1.19)	0.88	(0.51-1.51)	1.01	(0.60-1.68)	0.166

[1] Based on tests for trend across quintiles of meat consumption by assigning the median value of each quintile.

[2] Cox proportional hazard models adjusted for the same variables shown in the footnote of table 2.

Table 4.

Sex-specific multivariable hazard ratios (HR) and 95% confidence intervals (95% CI) of mortality from ischemic heart disease according to quintiles of total meat consumption stratified by BMI.

	Quintile of total meat consumption									
	Q1(low)	Q2		Q3		Q4		Q5(high)		*P* for
	reference	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	trend[1]
Men										
BMI <25 kg/m^2										
Person-Years	50578	52764		52929		53123		51803		
No. of subjects	3339	3384		3360		3379		3389		
No. of cases	49	56		51		36		40		
Multivariable HR[2]	1.00	1.23	(0.83-1.82)	1.12	(0.75-1.68)	0.78	(0.50-1.21)	0.75	(0.48-1.18)	0.048
BMI ≥25 kg/m^2										
Person-Years	12082	11543		11832		11282		11151		
No. of subjects	754	709		734		714		704		
No. of cases	25	9		12		13		10		
Multivariable HR[2]	1.00	0.39	(0.18-0.86)	0.52	(0.25-1.09)	0.61	(0.30-1.25)	0.36	(0.15-0.83)	0.043
Women										
BMI <25 kg/m^2										
Person-Years	76124	78615		79825		80296		79673		
No. of subjects	4826	4905		4953		4990		4965		
No. of cases	56	35		33		29		25		
Multivariable HR[2]	1.00	0.99	(0.64-1.53)	1.07	(0.68-1.67)	0.98	(0.61-1.57)	0.87	(0.52-1.45)	0.623
BMI ≥25 kg/m^2										
Person-Years	22733	21577		21093		20293		20761		
No. of subjects	1417	1339		1290		1254		1278		
No. of cases	17	9		6		6		20		
Multivariable HR[2]	1.00	0.64	(0.27-1.47)	0.58	(0.22-1.53)	0.53	(0.20-1.40)	2.04	(0.98-4.26)	0.040

[1] Based on tests for trend across quintiles of meat consumption by assigning the median value of each quintile.

[2] Cox proportional hazard models adjusted for the same variables shown in the footnote of table 2.

Supplemental Table 1.

Sex-specific hazard ratios (HR) and 95% confidence intervals (95% CI) of mortality from ischemic heart disease according to quintiles of each meat consumptions stratified by BMI among men (energy adjsuted).

	Quintile of each meat consumptions									
	Q1(low)	Q2		Q3		Q4		Q5(high)		*P* for
	reference	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	trend[1]
Men										
Red meat										
BMI <25 kg/m^2										
Person-Years	50238	52898		52760		53013		52289		
No. of subjects	3324	3385		3355		3371		3416		
No. of cases	46	59		44		49		34		
Multivariable HR[2]	1.00	1.37	(0.93-2.03)	1.06	(0.70-1.63)	1.17	(0.77-1.78)	0.71	(0.44-1.15)	0.065
BMI ≥25 kg/m^2										
Person-Years	12548	11349		11934		11353		10706		
No. of subjects	769	708		739		722		677		
No. of cases	23	15		9		10		12		
Multivariable HR[2]	1.00	0.90	(0.46-1.78)	0.47	(0.21-1.05)	0.61	(0.28-1.37)	0.64	(0.29-1.41)	0.204
Poultry										
BMI <25 kg/m^2										
Person-Years	52167	50826		54565		52671		50967		
No. of subjects	3382	3357		3377		3391		3344		
No. of cases	52	53		41		38		48		
Multivariable HR[2]	1.00	0.86	(0.56-1.33)	0.90	(0.58-1.40)	0.65	(0.40-1.05)	0.77	(0.51-1.18)	0.211
BMI ≥25 kg/m^2										
Person-Years	11258	11778		12467		11836		10552		
No. of subjects	672	738		774		735		696		
No. of cases	10	21		13		11		14		
Multivariable HR[2]	1.00	0.92	(0.40-2.14)	1.07	(0.45-2.58)	0.62	(0.25-1.53)	1.02	(0.47-2.23)	0.983
Processed meat										
BMI <25 kg/m^2										
Person-Years	53177	50415		50274		54256		53075		
No. of subjects	3386	3347		3365		3387		3366		
No. of cases	50	53		56		41		32		
Multivariable HR[2]	1.00	1.00	(0.62-1.61)	0.79	(0.47-1.32)	0.85	(0.54-1.34)	0.51	(0.30-0.85)	0.004
BMI ≥25 kg/m^2										
Person-Years	11422	11795		11235		11779		11659		
No. of subjects	707	746		729		706		727		
No. of cases	12	19		18		9		11		
Multivariable HR[2]	1.00	1.14	(0.45-2.87)	1.17	(0.42-3.23)	0.66	(0.26-1.70)	0.69	(0.25-1.91)	0.135
Liver										
BMI <25 kg/m^2										
Person-Years	55214	51121		52187		51986		50688		
No. of subjects	3421	3355		3320		3358		3397		
No. of cases	46	53		50		31		52		
Multivariable HR[2]	1.00	0.85	(0.52-1.41)	0.97	(0.63-1.50)	0.62	(0.36-1.04)	0.87	(0.56-1.38)	0.789
BMI ≥25 kg/m^2										
Person-Years	11591	11626		11418		11359		11896		
No. of subjects	711	736		717		702		749		
No. of cases	15	15		10		11		18		
Multivariable HR[2]	1.00	1.45	(0.53-3.98)	1.15	(0.47-2.85)	1.15	(0.41-3.18)	1.21	(0.45-3.21)	0.913

[1] Based on tests for trend across quintiles of meat consumption by assigning the median value of each quintile.

[2] Cox proportional hazard models adjusted for the same variables shown in the footnote of table 2.

Supplemental Table 2.

Sex-specific hazard ratios (HR) and 95% confidence intervals (95% CI) of mortality from ischemic heart disease according to quintiles of each meat consumptions stratified by BMI among women (energy adjsuted).

	Quintile of each meat consumptions									
	Q1(low)	Q2		Q3		Q4		Q5(high)		*P* for
	reference	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI	trend[1]
Women										
Red meat										
BMI <25 kg/m^2										
Person-Years	75531	78994		79864		80530		79612		
No. of subjects	4786	4898		4948		5011		4996		
No. of cases	59	40		24		26		29		
Multivariable HR[2]	1.00	1.07	(0.71-1.63)	0.76	(0.46-1.24)	0.92	(0.57-1.50)	1.06	(0.65-1.73)	0.995
BMI ≥25 kg/m^2										
Person-Years	23370	21798		21296		20061		19933		
No. of subjects	1457	1346		1295		1233		1247		
No. of cases	18	7		6		12		15		
Multivariable HR[2]	1.00	0.54	(0.22-1.32)	0.50	(0.19-1.30)	1.20	(0.54-2.63)	1.46	(0.68-3.14)	0.128
Poultry										
BMI <25 kg/m^2										
Person-Years	78194	77394		82905		77553		78486		
No. of subjects	4904	4931		5031		4907		4866		
No. of cases	37	45		28		38		30		
Multivariable HR[2]	1.00	1.17	(0.73-1.87)	1.20	(0.70-2.08)	1.15	(0.69-1.89)	0.98	(0.59-1.61)	0.743
BMI ≥25 kg/m^2										
Person-Years	21244	21149		19895		21521		22649		
No. of subjects	1339	1313		1212		1337		1377		
No. of cases	11	10		12		12		13		
Multivariable HR[2]	1.00	0.83	(0.32-2.14)	1.44	(0.58-3.59)	0.94	(0.37-2.40)	1.29	(0.55-3.01)	0.431
Processed meat										
BMI <25 kg/m^2										
Person-Years	79407	76129		76865		81381		80750		
No. of subjects	4947	4896		4912		4928		4956		
No. of cases	35	50		48		20		25		
Multivariable HR[2]	1.00	1.19	(0.67-2.12)	0.93	(0.51-1.72)	0.78	(0.43-1.42)	0.88	(0.48-1.59)	0.345
BMI ≥25 kg/m^2										
Person-Years	20749	21572		21031		21965		21140		
No. of subjects	1296	1348		1331		1316		1287		
No. of cases	9	10		15		12		12		
Multivariable HR[2]	1.00	0.82	(0.28-2.39)	1.36	(0.43-4.27)	1.25	(0.49-3.19)	1.19	(0.44-3.25)	0.665
Liver										
BMI <25 kg/m^2										
Person-Years	82265	77913		76610		80050		77694		
No. of subjects	4937	4875		4875		4981		4971		
No. of cases	33	46		42		23		34		
Multivariable HR[2]	1.00	1.10	(0.54-2.27)	0.54	(0.27-1.08)	0.91	(0.48-1.72)	0.69	(0.37-1.29)	0.663
BMI ≥25 kg/m^2										
Person-Years	21564	22482		22096		20470		19846		
No. of subjects	1306	1369		1368		1263		1272		
No. of cases	9	8		13		8		20		
Multivariable HR[2]	1.00	0.50	(0.15-1.71)	1.25	(0.38-4.08)	0.84	(0.28-2.48)	2.34	(0.88-6.24)	0.001

[1] Based on tests for trend across quintiles of meat consumption by assigning the median value of each quintile.

[2] Cox proportional hazard models adjusted for the same variables shown in the footnote of table 2.