

Red meat consumption is associated with the risk of type 2 diabetes in men but not in women: a Japan Public Health Center-based Prospective Study

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Abstract

The relationship between different types of meat intake and the risk of type 2 diabetes remains unclear. We prospectively examined the association between total meat, total red meat, unprocessed red meat, processed meat and poultry intake and the incidence of type 2 diabetes. Subjects were 27 425 men and 36 424 women aged 45–75 years who participated in the second survey of the Japan Public Health Center-based Prospective Study, and had no history of type 2 diabetes, cancer, stroke, IHD, chronic liver disease or kidney disease. Meat intake was estimated using a validated 147-item FFQ. OR of self-reported, physician-diagnosed type 2 diabetes over 5 years were estimated using a multiple logistic regression. A total of 1178 newly diagnosed cases of type 2 diabetes were self-reported. Intakes of total meat and total red meat were associated with the increased risk of type 2 diabetes in men but not in women. The multivariate-adjusted OR for the highest quartile compared with the lowest quartile of total meat and total red meat intake were 1.36 (95% CI 1.07, 1.73; *P* for trend=0.006) and 1.48 (95% CI 1.15, 1.90; *P* for trend=0.003) for men, respectively, and 0.82 (95% CI 0.62, 1.09; *P* for trend=0.14) and 0.77 (95% CI 0.57, 1.02; *P* for trend=0.08) for women, respectively. Intakes of processed red meat and poultry were not associated with the increased risk of diabetes in either men or women. In conclusion, elevated intake of red meat is associated with the increased risk of type 2 diabetes in Japanese men but not in women.

Key words: Meats: Red meat: Processed meats: Poultry: Type 2 diabetes

The incidence of diabetes has been increasing globally, with an estimated world prevalence reaching 7.7% by 2030⁽¹⁾. In Japan, the prevalence of diabetes has increased markedly over the last few decades⁽²⁾, and it has been argued that the increase is primarily due to the Westernisation of diet, including the increased intake of animal products⁽³⁾. Data from prospective studies have indicated that total meat intake is consistently associated with the increased risk of type 2 diabetes among men^(4–6), whereas inconsistent findings have been observed in women^(4,7). The results of recent meta-analyses of prospective studies support that a high red meat^(8,9) and processed meat^(8–10) intake increases

the risk of type 2 diabetes in both men and women. Fe, which is contained in red meat, may play a role as a mediator of the adverse effect of red meat intake on glucose metabolism^(11,12). Additionally, SFA in meat may increase inflammatory response and secondarily enhance the risk of type 2 diabetes⁽¹³⁾. In terms of poultry intake, cohort studies have reported no association among men^(4–6,14,15), but data among women are conflicting^(4,7,14–16).

Epidemiological evidence on this issue is limited among Asian populations, in which meat consumption is much lower than that in Western populations⁽¹⁷⁾. In a study of Chinese women, the only prospective investigation in Asia, intake of total meat

Abbreviation: JPHC, Japan Public Health Center-based Prospective.

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(red meat and poultry), was inversely associated with the risk of type 2 diabetes⁽⁷⁾, a finding that conflicts with the findings of Western studies^(4–6,18), although the association between processed meat intake and the risk of type 2 diabetes in the Chinese study⁽⁷⁾ is consistent with those in Western studies^(4,5,14–16,19–23). Japanese patients with type 2 diabetes are on average leaner than their Western counterparts⁽²⁴⁾, and Japanese-Americans have lower β -cell function than do non-Hispanic whites⁽²⁵⁾. Thus, the effect of meat consumption on type 2 diabetes in the Japanese population may differ from the effect in Western populations. Here, we prospectively investigated the association between meat intake (total red meat, unprocessed red meat, processed red meat and poultry) and the risk of type 2 diabetes in a large-scale, population-based cohort of Japanese men and women. Further, we examined the association by BMI, which is a major predictor of type 2 diabetes risk, and by menopausal status (women only), which is a determinant of body Fe storage that may increase with the intake of Fe-containing foods including meat, and which has been linked to type 2 diabetes risk⁽²⁶⁾.

Materials and methods

Study design

Cohort I of the Japan Public Health Center-based Prospective (JPHC) Study was established in 1990, and cohort II was established in 1993⁽²⁷⁾. The study protocol was approved by the institutional review board of the National Cancer Center, Tokyo, Japan. The participants of cohort I included residents aged 40–59 years in five Japanese public health centre areas (Iwate, Akita, Nagano, Okinawa and Tokyo). The participants of cohort II included residents aged 40–69 years in six public health centre areas (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa and Osaka). Although we did not require written informed consent, the study participants were informed of the objectives of the study, and participants who responded to the questionnaire survey were considered to have consented to participate in the survey.

Among the baseline subjects (n 140 420), 113 403 subjects responded to the questionnaire survey at baseline. Of these, 89 947 (79.3%) subjects responded to the 5-year follow-up survey (second survey). Of these subjects, 76 901 (67.8%) responded to the 10-year follow-up survey (third survey). We excluded 12 462 subjects who reported a history of type 2 diabetes, cancer, stroke, IHD and chronic liver disease at baseline or at the second survey, as well as those who reported kidney disease at the baseline survey. Individuals who were missing information regarding their meat intake were excluded. We also excluded 590 subjects who reported extreme total energy intakes (outside of the mean ± 3 SD according to sex). Finally, a total of 63 849 subjects (27 425 men and 36 424 women) remained in the present analysis.

FFQ

Participants completed a self-administered FFQ at the baseline, second and third surveys. The data included 147 food

and beverage items and nine frequency categories⁽²⁸⁾. For the present analysis, we used data from the second survey as the baseline data because the questionnaire used for the second survey more comprehensively inquired about food intakes than the one used for the baseline survey. At the second survey, we asked about the usual consumption of sixteen meat items over the past year⁽²⁸⁾. The red meat items included three beef dishes (steak, grilled beef and stewed beef), six pork dishes (stir-fried pork, deep-fried pork, stewed pork in the Western style, stewed pork in the Japanese style, pork in soup and pork liver), four processed meat products (ham, sausage or Wiener sausage, bacon and luncheon meat) and chicken liver. Poultry items included two chicken meals (grilled chicken and deep-fried chicken). For most food items, nine response options were available to describe consumption frequency, ranging from rarely (<1 time/month) to ≥ 7 times/d. A standard portion size was specified for each food, and respondents were asked to choose their usual portion size from three options (≤ 0.5 times, standard or ≥ 1.5 times). The daily intake of meat and meat products was calculated by multiplying the daily consumption frequency by the typical portion size, and was expressed as g/d. These individual items were categorised into five main groups of total meat, total red meat (unprocessed and processed red meat items), unprocessed red meat, processed red meat and poultry.

Referring to the Standard Tables of Food Composition in Japan⁽²⁹⁾, dietary intakes for energy and selected nutrients were estimated. The validity and reproducibility of the FFQ was examined in a subsample of the participants in the JPHC Study cohort I and cohort II. Details of the validation study have been described elsewhere^(30–32). For the validity of the FFQ, energy-adjusted Spearman's correlation coefficients between intake values for meat derived from the FFQ and those derived from 28 or 14 d dietary records were 0.50 for men and 0.45 for women, respectively, for cohort I⁽³²⁾, and 0.48 for men and 0.44 for women, respectively, for cohort II⁽³⁰⁾. With regard to the reproducibility of the FFQ, energy-adjusted Spearman's correlation coefficients for intake of meat derived from the two FFQ administered 1 year apart were 0.52 for both men and women for cohort I⁽³¹⁾ and 0.52 for men and 0.41 for women, respectively, for cohort II⁽³⁰⁾.

Ascertainment of type 2 diabetes

Type 2 diabetes was ascertained using a self-administered questionnaire. At the third survey, study participants were asked about their history of major diseases including diabetes and, if it was present, the timing of the initial diagnosis in relation to the first and second surveys. Because the 5-year survey was used as the baseline measure in the present study, only participants who were subsequently diagnosed were regarded as incident cases during the follow-up. Details regarding the assessment of the validity of self-reported diabetes have been described elsewhere⁽³³⁾. Previously, we showed that 94% of self-reported diabetes cases were confirmed by medical records.

Statistical analyses

Analyses of men and women were performed separately. Participants were divided into intake quartiles. The confounding variables considered were as follows: age (years, continuous); study area (eleven areas); BMI (<21, 21–22.9, 23–24.9, 25–26.9 or ≥ 27 kg/m²); smoking status (lifetime non-smoker, former smoker or current smoker with a consumption of either <20 or ≥ 20 cigarettes/d); alcohol consumption (non-drinker, occasional drinker or drinker with a consumption of <150, 150–299, 300–499 or ≥ 450 g ethanol/week for men and <150 or ≥ 150 g ethanol/week for women); total physical activity level (metabolic equivalent-h/d, quartiles); history of hypertension (yes or no); family history of diabetes mellitus (yes or no); coffee consumption (almost never, <1, 1 or ≥ 2 cups/d); total energy intake (kJ/d, continuous); Ca intake (mg/d, continuous); Mg intake (mg/d, continuous); rice intake (g/d, continuous); fish intake (g/d, continuous); vegetable intake (g/d, continuous); soft drink intake (g/d, continuous). The dietary factors considered here have been shown to be associated with the risk of type 2 diabetes both in previous studies and in the present cohort. An indicator variable for missing data was created for each covariate. Trend associations between confounding factors and meat intakes were examined using the Mantel–Haenszel χ^2 test for categorical variables and linear regression analysis for continuous variables.

The association between the intakes of energy-adjusted total meat, total red meat, unprocessed red meat, processed red meat or poultry and the risk of diabetes was assessed by OR, which were estimated using a multiple logistic regression. A 95% CI of the OR was estimated using the Wald method. The first model was adjusted for age and study area, and the second was further adjusted for BMI, smoking status, alcohol consumption, the family history of diabetes mellitus, the history of hypertension, total physical activity level, total energy intake, coffee consumption and the intakes of Ca, Mg, rice, fish, vegetables and soft drinks. An additional model was further adjusted for Fe intake (g/d, continuous) or saturated fat intake (g/d, continuous). The trend association was assessed by assigning the ordinal numbers 0–3 to the four categories of each meat or specific groups of meat consumption. We also analysed data by BMI (<25 or ≥ 25 kg/m²) in both men and women and menopausal status (pre-menopausal or postmenopausal) in women. An interaction term of dietary intake (continuous) and the above stratifying variables (dichotomous) was created and added to the model to assess statistical interactions. Statistical significance was declared if the two-sided *P* value was less than 0.05. All analyses were performed using SAS software (version 9.2; SAS Institute).

Results

During the 5-year period, 1178 participants (681 men and 497 women) were newly self-reported as having type 2 diabetes. At baseline (the time of the second survey), both men and women with higher intakes of total meat were more likely to be young and to have a high BMI. They also had

higher intakes of protein, fat, soft drinks and coffee, and lower intakes of carbohydrates, Ca, Mg, rice and vegetable than those with lower total meat intakes (Table 1). Men who consumed greater amounts of total meat were less likely to report higher levels of physical activity at work or during leisure time and to consume alcohol.

Total meat was positively associated with the risk of type 2 diabetes in men (Table 2). The OR in the highest quartile of total meat intake compared with those in the lowest was 1.36 (95% CI 1.07, 1.73; *P* for trend=0.006) in the multivariate-adjusted model. The median intake of total red meat was 45.6 and 40.1 g/d in men and women, respectively. High intakes of total red meat and unprocessed red meat were statistically significantly associated with an increased risk of type 2 diabetes in men. The multivariate-adjusted OR of type 2 diabetes for the lowest to the highest quartile category of intake were 1.00 (reference), 1.09 (95% CI 0.87, 1.37), 1.15 (95% CI 0.91, 1.46) and 1.48 (95% CI 1.15, 1.90) (*P* for trend=0.003) and 1.00 (reference), 0.99 (95% CI 0.79, 1.24), 1.01 (95% CI 0.80, 1.27) and 1.42 (95% CI 1.12, 1.80) (*P* for trend=0.007) for total red meat and unprocessed red meat, respectively. These associations were only slightly attenuated after additional adjustment for Fe intake. We did not observe significant associations of total red meat and unprocessed red meat with the risk of type 2 diabetes in women. Poultry consumption was not associated with the risk of type 2 diabetes among either men or women. In stratified analyses, there was no significant interaction by BMI or menopausal status (women only).

Discussion

In the present large-scale population-based prospective study in Japanese adults, a high consumption of total meat, total red meat and unprocessed red meat were associated with the increased risk of type 2 diabetes in men but not in women. Processed red meat and poultry intakes were not associated with an increased risk of diabetes in men or women. Thus, the associations with total meat and total red meat are largely accounted for by the association with unprocessed red meat.

The present finding of a positive association of total meat intake with the risk of type 2 diabetes in men is consistent with a recent meta-analysis of three cohort studies from the USA; the summary relative risk of type 2 diabetes per 100 g/d of total meat was 1.12 (95% CI 1.05, 1.19)⁽¹⁰⁾. Although another meta-analysis of five prospective studies from the USA, Australia, Japan and China reported no clear association of total meat intake with the risk of type 2 diabetes, a statistically significantly increased risk associated with a high intake of total meat emerged after excluding a Chinese study⁽⁷⁾; the summary relative risk of type 2 diabetes comparing a high *v.* low intake of total meat was 1.31 (95% CI 1.12, 1.52)⁽⁸⁾. In contrast, the present study found no association in women, a finding that is inconsistent with those found for women in a Western study⁽⁴⁾. The above-mentioned study in Chinese women reported a decreased, rather than increased, risk of type 2 diabetes associated with a higher intake of total meat. Although caution needs to be exercised

Table 1. Baseline characteristics of the subjects according to categories of energy-adjusted meat intake*
(Mean values and standard deviations; percentages)

	Quartiles of total meat intake							
	Q1		Q2		Q3		Q4	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Men								
<i>n</i>	6856		6856		6857		6856	
Age (years)†	52.2	7.5	51.0	7.7	50.5	7.7	50.7	7.8
BMI (kg/m ²)†	23.4	2.7	23.5	2.8	23.6	2.8	23.8	2.9
Current smoker (%)†	44.5		46.9		46.0		44.0	
Alcohol consumption ≥ 1 d/week (%)†	71.3		71.2		68.6		58.5	
Total physical activity (MET-h/d)†	34.2	6.8	34.1	6.8	33.8	6.7	33.7	6.7
History of hypertension (%)†	18.4		17.3		16.1		15.9	
Family history of diabetes (%)	8.7		8.0		8.3		7.8	
Food and nutrient intake‡								
Energy (kJ/d)†	9532	3156	9473	2901	9385	2951	9146	3282
Protein (g/d)†	68	15	71	13	73	12	77	12
Carbohydrate (g/d)†	300	53	291	45	279	42	251	43
Fat (g/d)†	44	14	50	12	56	11	70	15
Saturated fat (g/d)†	13	6	15	5	17	4	21	5
Monounsaturated fat (g/d)†	14	4	17	4	20	4	26	6
Polyunsaturated fat (g/d)†	11	4	12	3	13	3	15	3
Ca (mg/d)†	543	274	512	216	486	192	448	179
Mg (mg/d)†	288	63	283	53	278	49	265	50
Fe (mg/d)	9.1	2.5	9.0	2.1	9.0	2.1	9.1	2.2
Rice (g/d)†	470	195	455	172	430	155	374	146
Vegetables (g/d)†	198	146	197	121	194	119	190	115
Fish (g/d)†	87	61	90	51	93	49	92	52
Soft drinks (g/d)†	42	242	49	195	59	220	90	326
Coffee consumption ≥ 1 cup/d (%)†	29.1		32.3		34.5		32.9	
Women								
<i>n</i>	9106		9106		9106		9106	
Age (years)†	52.6	7.7	51.5	7.7	51.0	7.8	51.1	8.0
BMI (kg/m ²)†	23.4	3.1	23.4	3.0	23.4	3.1	23.7	3.2
Current smoker (%)†	4.4		4.0		4.1		5.1	
Alcohol consumption ≥ 1 d/week (%)	11.4		13.9		13.2		10.7	
Total physical activity (MET-h/d)	32.9	5.7	32.9	5.7	32.9	5.7	32.8	5.8
History of hypertension (%)†	20.5		17.9		17.2		18.1	
Family history of diabetes (%)†	9.1		9.2		9.0		7.8	
Postmenopausal status (%)†	78.3		73.9		70.4		63.2	
Food and nutrient intake‡								
Energy (kJ/d)†	8251	2972	8092	2620	8037	2541	7790	2754
Protein (g/d)†	67	11	68	10	69	9	71	10
Carbohydrate (g/d)†	275	35	263	29	250	26	224	32
Fat (g/d)†	47	11	52	10	56	9	67	13
Saturated fat (g/d)†	14	5	16	4	17	4	20	5
Monounsaturated fat (g/d)†	15	4	17	3	19	3	24	5
Polyunsaturated fat (g/d)†	12	3	12	3	13	3	14	3
Ca (mg/d)†	616	254	571	201	530	177	468	179
Mg (mg/d)†	289	55	277	45	268	42	250	47
Fe (mg/d)†	9.2	2.3	9.0	1.9	8.9	1.9	8.7	2.0
Rice (g/d)†	361	153	354	133	346	126	313	122
Vegetables (g/d)†	249	159	236	126	222	115	206	119
Fish (g/d)	85	55	86	46	88	43	85	47
Soft drinks (g/d)†	12	56	15	67	17	66	26	95
Coffee consumption ≥ 1 cup/d (%)†	32.8		37.1		36.6		34.8	

MET, metabolic equivalents.

* On the basis of the Mantel-Haenszel χ^2 test for categorical variables and linear regression analysis for continuous variables with the assignment of ordinal numbers 0–3 to the categories of total meat intake.

† *P* for trend < 0.05.

‡ Energy adjusted by the residual method except for energy intake and coffee consumption.

when interpreting the results of the Chinese study, as their measure of total meat included unprocessed red meat and poultry but not processed meat⁽⁷⁾, available evidence from Japan and China did not support the hypothesis that total

meat intake is associated with the increased risk of type 2 diabetes among female Asian populations.

The present finding of a positive association with the consumption of total red meat, which is mainly derived from

Table 2. Type 2 diabetes according to the quartile categories of energy-adjusted meat intakes (Odds ratios and 95% confidence intervals)

	Quartile category						<i>P</i> for trend*		
	Q1		Q2		Q3			Q4	
	OR	OR	95% CI	OR	95% CI	OR		95% CI	
Men									
Total meat									
Cases/subjects (<i>n</i>)	166/6856		143/6856		168/6857		204/6856		
Median (g)	23.2		44.8		67.2		107.8		
Age- and area-adjusted OR†	1.00 (reference)	0.87	0.69, 1.09	1.03	0.83, 1.29	1.26	1.02, 1.57	0.01	
Multivariate-adjusted OR‡	1.00 (reference)	0.88	0.70, 1.11	1.06	0.85, 1.34	1.36	1.07, 1.73	0.006	
Plus Fe-adjusted OR‡	1.00 (reference)	0.88	0.70, 1.11	1.06	0.84, 1.33	1.33	1.05, 1.70	0.01	
Plus saturated fat-adjusted OR‡	1.00 (reference)	0.89	0.71, 1.13	1.10	0.85, 1.41	1.44	1.05, 1.99	0.03	
Total red meat									
Cases/subjects (<i>n</i>)	152/6856		161/6856		166/6857		202/6856		
Median (g)	17.9		36.5		56.4		94.9		
Age- and area-adjusted OR†	1.00 (reference)	1.08	0.86, 1.35	1.12	0.89, 1.40	1.38	1.10, 1.72	0.006	
Multivariate-adjusted OR‡	1.00 (reference)	1.09	0.87, 1.37	1.15	0.91, 1.46	1.48	1.15, 1.90	0.003	
Plus Fe-adjusted OR‡	1.00 (reference)	1.09	0.86, 1.36	1.14	0.90, 1.44	1.45	1.13, 1.86	0.005	
Plus saturated fat-adjusted OR‡	1.00 (reference)	1.11	0.88, 1.40	1.19	0.92, 1.54	1.58	1.14, 2.20	0.01	
Unprocessed red meat									
Cases/subjects (<i>n</i>)	160/6856		157/6856		157/6857		207/6856		
Median (g)	15.1		31.4		49.0		82.7		
Age- and area-adjusted OR†	1.00 (reference)	0.99	0.79, 1.24	1.00	0.80, 1.25	1.33	1.07, 1.65	0.01	
Multivariate-adjusted OR‡	1.00 (reference)	0.99	0.79, 1.24	1.01	0.80, 1.27	1.42	1.12, 1.81	0.007	
Plus Fe-adjusted OR‡	1.00 (reference)	0.99	0.79, 1.24	1.00	0.79, 1.26	1.39	1.09, 1.77	0.01	
Plus saturated fat-adjusted OR‡	1.00 (reference)	1.01	0.80, 1.27	1.04	0.81, 1.33	1.51	1.10, 2.06	0.03	
Processed red meat									
Cases/subjects (<i>n</i>)	167/6856		167/6856		155/6857		192/6856		
Median (g)	0.0		2.4		5.6		14.6		
Age- and area-adjusted OR†	1.00 (reference)	1.02	0.82, 1.28	0.95	0.76, 1.20	1.19	0.94, 1.51	0.24	
Multivariate-adjusted OR‡	1.00 (reference)	1.02	0.81, 1.27	0.94	0.75, 1.19	1.19	0.94, 1.50	0.27	
Plus Fe-adjusted OR‡	1.00 (reference)	1.02	0.82, 1.27	0.94	0.75, 1.19	1.18	0.93, 1.49	0.30	
Plus saturated fat-adjusted OR‡	1.00 (reference)	1.01	0.81, 1.26	0.93	0.74, 1.17	1.15	0.90, 1.46	0.43	
Poultry									
Cases/subjects (<i>n</i>)	168/6856		149/6856		178/6857		186/6856		
Median (g)	0.0		5.1		9.6		20.1		
Age- and area-adjusted OR†	1.00 (reference)	0.90	0.72, 1.12	1.08	0.87, 1.34	1.12	0.91, 1.39	0.12	
Multivariate-adjusted OR‡	1.00 (reference)	0.87	0.69, 1.09	1.02	0.82, 1.27	1.07	0.85, 1.34	0.38	
Plus Fe-adjusted OR‡	1.00 (reference)	0.87	0.69, 1.09	1.01	0.81, 1.26	1.06	0.84, 1.33	0.41	
Plus saturated fat-adjusted OR‡	1.00 (reference)	0.86	0.68, 1.08	0.99	0.80, 1.24	1.03	0.81, 1.30	0.59	
Women									
Total meat									
Cases/subjects (<i>n</i>)	140/9106		127/9106		115/9106		115/9106		
Median (g)	19.9		39.4		59.2		94.4		
Age- and area-adjusted OR†	1.00 (reference)	0.94	0.73, 1.19	0.85	0.67, 1.10	0.82	0.64, 1.07	0.10	
Multivariate-adjusted OR‡	1.00 (reference)	0.97	0.76, 1.25	0.89	0.68, 1.15	0.82	0.62, 1.09	0.14	
Plus Fe-adjusted OR‡	1.00 (reference)	0.97	0.76, 1.25	0.89	0.69, 1.15	0.83	0.62, 1.10	0.15	
Plus saturated fat-adjusted OR‡	1.00 (reference)	1.05	0.81, 1.36	1.03	0.77, 1.37	1.11	0.76, 1.62	0.68	
Total red meat									
Cases/subjects (<i>n</i>)	143/9106		124/9106		118/9106		112/9106		
Median (g)	15.2		32.0		49.5		82.9		
Age- and area-adjusted OR†	1.00 (reference)	0.90	0.70, 1.14	0.86	0.67, 1.10	0.77	0.60, 1.01	0.052	
Multivariate-adjusted OR‡	1.00 (reference)	0.93	0.73, 1.19	0.89	0.69, 1.15	0.77	0.57, 1.02	0.08	
Plus Fe-adjusted OR‡	1.00 (reference)	0.93	0.73, 1.20	0.89	0.69, 1.16	0.77	0.57, 1.03	0.08	
Plus saturated fat-adjusted OR‡	1.00 (reference)	0.99	0.77, 1.28	1.01	0.76, 1.35	0.99	0.67, 1.45	0.99	
Unprocessed red meat									
Cases/subjects (<i>n</i>)	137/9106		133/9106		115/9106		112/9106		
Median (g)	12.3		26.9		42.4		72.2		
Age- and area-adjusted OR†	1.00 (reference)	1.00	0.79, 1.27	0.87	0.67, 1.11	0.81	0.62, 1.05	0.06	
Multivariate-adjusted OR‡	1.00 (reference)	1.04	0.82, 1.33	0.91	0.71, 1.18	0.81	0.61, 1.07	0.10	
Plus Fe-adjusted OR‡	1.00 (reference)	1.04	0.82, 1.33	0.92	0.71, 1.19	0.81	0.61, 1.08	0.11	
Plus saturated fat-adjusted OR‡	1.00 (reference)	1.11	0.86, 1.43	1.03	0.76, 1.37	1.04	0.72, 1.50	0.90	
Processed red meat									
Cases/subjects (<i>n</i>)	140/9106		116/9106		125/9106		116/9106		
Median (g)	0.0		2.4		5.6		13.5		
Age- and area-adjusted OR†	1.00 (reference)	0.89	0.69, 1.14	0.98	0.76, 1.25	0.90	0.70, 1.17	0.61	
Multivariate-adjusted OR‡	1.00 (reference)	0.94	0.73, 1.22	1.05	0.82, 1.36	0.96	0.73, 1.26	0.98	
Plus Fe-adjusted OR‡	1.00 (reference)	0.94	0.73, 1.22	1.05	0.82, 1.36	0.96	0.73, 1.27	1.00	
Plus saturated fat-adjusted OR‡	1.00 (reference)	0.97	0.75, 1.26	1.11	0.86, 1.43	1.05	0.79, 1.40	0.53	

Table 2. *Continued*

	Quartile category								<i>P</i> for trend*
	Q1		Q2		Q3		Q4		
	OR		OR	95% CI	OR	95% CI	OR	95% CI	
Poultry	139/9106		109/9106		125/9106		124/9106		
Cases/subjects (<i>n</i>)	0.0		4.5		8.6		17.8		
Median (g)	1.00 (reference)		0.80 0.62, 1.03		0.93 0.73, 1.19		0.91 0.71, 1.17		0.72
Age- and area-adjusted OR†	1.00 (reference)		0.82 0.63, 1.05		0.94 0.73, 1.21		0.89 0.68, 1.15		0.56
Multivariate-adjusted OR‡	1.00 (reference)		0.82 0.63, 1.05		0.94 0.73, 1.21		0.89 0.68, 1.16		0.58
Plus Fe-adjusted OR‡	1.00 (reference)		0.84 0.65, 1.09		0.99 0.77, 1.28		0.97 0.74, 1.27		0.94
Plus saturated fat-adjusted OR‡	1.00 (reference)		0.84 0.65, 1.09		0.99 0.77, 1.28		0.97 0.74, 1.27		0.94

* Trend association was assessed by assigning the ordinal numbers 0–3 to the four categories of each meat or specific groups of meat consumption.

† Adjusted for age and public health centre area.

‡ Additionally adjusted for BMI, smoking status, alcohol consumption, total physical activity, the history of hypertension, coffee consumption, the family history of diabetes, Mg intake, Ca intake, rice intake, fish intake, vegetable intake, soft drink consumption and energy intake.

the association with unprocessed red meat, is consistent with the result of two meta-analyses of data from prospective studies that were mainly conducted in Western populations (pooled hazard ratio 1.21, 95% CI 1.07, 1.38⁽⁸⁾ and pooled hazard ratio 1.19, 95% CI 1.04, 1.37 for 100 g/d⁽⁹⁾). However, the absolute amount of total red meat intake in the present study population (median 45.6 and 40.1 g/d in men and women, respectively) was lower than that in the US population (mean 69.8 g/d)⁽³⁴⁾, but was similar to that in the Chinese study population (median 42.6 g/d)⁽⁷⁾. Additionally, the type of unprocessed red meat consumed was considerably different among studies: pork intake was almost twice as high as beef intake in the USA⁽³⁵⁾ and in the present study population, while in the Chinese study population, pork was consumed much more often than beef (9:1)⁽⁷⁾. Given that the Chinese study showed no increased risk of type 2 diabetes⁽⁷⁾, beef intake might have a stronger influence on the risk of type 2 diabetes than pork intake. In fact, a randomised controlled trial has suggested that a regular intake of pork in place of other meats improves body composition⁽³⁶⁾.

A positive association between processed meat and type 2 diabetes has been observed in three meta-analyses of cohort studies^(8–10) and in prospective studies^(4,5,14,15,20) that were not included in those meta-analyses. The magnitudes of increases in risk associated with processed meat intake were greater than those associated with red meat intake^(8–10). For example, there were 41 and 21% increased risks for the highest *v.* lowest intake of processed meat and red meat, respectively⁽⁸⁾. In the present study, however, men in the highest quartile of processed meat intake had a statistically insignificant 15% increased risk of type 2 diabetes compared with those in the lowest quartile. One explanation for this discrepancy is that processed meat consumption in Japan is much lower than in the USA (mean 12.4 g/d in Japan and 23.2 g/d in the USA)^(34,37). In the present study population, the median in the highest quartile of processed red meat consumption was 13.1 g/8368 kJ (2000 kcal) per d among men and 14.1 g/8368 kJ (2000 kcal) per d among women. Similarly, in the Multiethnic Cohort in Hawaii, Japanese-American men and women in the highest category of processed red

meat intake (17.1 g/8368 kJ (2000 kcal) per d in men and 13.9 g/8368 kJ (2000 kcal)/d in women) showed only modest increases in the risk of type 2 diabetes (24 and 23% for men and women, respectively) compared with those with the lowest category of meat intake⁽¹⁵⁾. Few Japanese are likely to consume processed red meat above the level that is apparently associated with the increased risk of type 2 diabetes.

Poultry intake was not appreciably associated with the risk of type 2 diabetes among either men or women in the present study. Previously, no association between poultry intake and the risk of type 2 diabetes has been consistently reported in men^(4–6,14,15). In women, however, data have been mixed^(4,7,14–16), with two studies showing a decrease^(7,16), one study showing no association⁽¹⁵⁾ and two studies showing an increase in the risk of type 2 diabetes^(4,14). Given that the majority of these studies did not detect an increased risk of type 2 diabetes associated with poultry intake, poultry intake may not impair glucose metabolism. There are some possible explanations. As poultry contains a lower amount of haem Fe than red meat, a higher intake of poultry may not significantly increase Fe storage, which has been linked to the risk of type 2 diabetes⁽³⁸⁾. Moreover, PUFA in poultry can improve insulin sensitivity⁽³⁹⁾.

In the present study, intakes of total meat, red meat and unprocessed red meat were associated with the risk of type 2 diabetes in men only. This could be ascribed, at least in part, to sex difference in Fe storage, which increases with the intake of Fe-rich foods including red meat. Circulating ferritin concentrations (a marker of Fe storage) in pre-menopausal women are much lower than those in men⁽³⁸⁾, and showed no association with insulin resistance^(40,41). In post-menopausal women, whose blood ferritin levels are also lower than those in men⁽³⁸⁾, studies on insulin resistance have yielded mixed results, with one US study reporting a positive association with ferritin concentrations⁽⁴¹⁾, whereas a Korean study reported no association⁽⁴⁰⁾. In the present study, no increase in the risk of type 2 diabetes with a high intake of meat was observed among either pre- or postmenopausal women. The present finding may be supported by a Japanese study, in which serum ferritin concentrations were

significantly associated with an insulin resistance marker in men but not in women⁽⁴²⁾. For Asian women, meat intake may not increase Fe storage to the level above which glucose metabolism is impaired.

The mechanism underlying the association between meat intake and the risk of type 2 diabetes is unclear. Haem Fe in red meat has been suggested to play an unfavourable role in glucose metabolism⁽³⁸⁾. Fe is a strong pro-oxidant and pro-inflammatory factor that catalyses several reactions leading to the formation of reactive oxygen species and resulting in elevated oxidative stress and inflammation⁽⁴³⁾, which may decrease insulin sensitivity^(38,44). Increased Fe stores in the liver may induce insulin resistance by impeding the capacity for insulin extraction⁽³⁸⁾. Fe impairs insulin action and interferes with glucose uptake in adipocytes⁽³⁸⁾. In addition, increased muscle Fe stores enhance NEFA oxidation and cause them to interfere with glucose disposal⁽³⁸⁾. Excess body Fe causes Fe deposition in pancreatic β -cells, resulting in impaired insulin secretion⁽³⁸⁾. In epidemiological studies, intake of haem Fe has been consistently associated with an increased risk of type 2 diabetes⁽³⁸⁾. In the present study, however, adjustment for Fe intake only slightly attenuated the association between total meat and total red meat and the risk of type 2 diabetes, indicating that mechanisms other than the latter may exist. Meat is also a major source of saturated fat, which is increased in cell membranes and leads to decreased membrane fluidity and decreased insulin receptor affinity⁽⁴⁵⁾. Saturated fat increases inflammatory responses and secondarily enhances the risk of type 2 diabetes⁽¹³⁾. However, the adjustment for saturated fat intake did not appreciably change the result in the present study. Alternatively, advanced glycation end products and heterocyclic amines, which are formed in meat through heating and processing^(46,47), have been shown to increase oxidative stress and inflammation, leading to the progression of insulin resistance in mice⁽⁴⁸⁾. In a study of patients with type 2 diabetes, restriction of dietary advanced glycation end products improved insulin sensitivity⁽⁴⁹⁾.

The major strengths of the present study include a large number of male and female participants, the population-based prospective design, the use of a validated FFQ and adjustment for or stratification by potentially important confounding variables. Limitations of the present study also deserve mention. First, the diagnosis of type 2 diabetes was ascertained via self-report. We confirmed that 94% of self-reported diabetes cases were correctly documented in medical records in a sample of a validation study⁽³³⁾, but undiagnosed cases may exist. It is unlikely, however, that the probability of under-diagnosis differs according to meat intake, and the use of self-reported data might not have substantially influenced the risk estimate. Second, we used only 5-year survey data for the assessment of dietary intake. Due to random variation, this would lead to a non-differential misclassification of meat intake and would thus distort the OR towards the null. In addition, one-time dietary measurement at baseline may not capture long-term intake, which is relevant to the development of type 2 diabetes. Repeated assessment of the diet over a long period of time before disease onset will probably

provide a better estimate of exposure status. Third, although the validity of the FFQ for meat intake was relatively high (r 0.44–0.50), the measurement error in the FFQ might result in biased associations between meat intake and the risk of type 2 diabetes, which would drive the results towards the null. Fourth, we adjusted for dietary Fe intake but not for blood ferritin concentration, which is a better marker of body Fe status. Fifth, the follow-up period was relatively short (5 years). Finally, we could not rule out the possibility of unmeasured and residual confounding.

In conclusion, we found that total red meat and unprocessed red meat intakes were associated with the increased risk of type 2 diabetes after adjustment for other risk factors for type 2 diabetes among Japanese men, whose meat consumption is lower than that of Westerners. The present study adds to the evidence showing the adverse effect of high meat consumption on glucose metabolism.

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