Relation of unprocessed, processed red meat and poultry consumption to blood pressure in East Asian and Western adults

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Abstract

Background: Epidemiologic evidence suggests that relationships of red meat consumption with risk of cardiovascular diseases depends on whether or not the meat is processed, including addition of preservatives, but evidence is limited for blood pressure (BP).

Objective: To examine cross-sectional associations with BP of unprocessed and processed red meat and poultry consumption, total and by type, using data from the INTERnational study on MAcro/micronutrients and blood Pressure (INTERMAP).

Design: INTERMAP included 4,680 men and women ages 40-59 years from 17 population samples in Japan, China, the United Kingdom, and the United States. During four visits, eight BP measurements, four multi-pass 24-hr dietary recalls, and two timed 24-hr urine samples were collected.

Results: Average daily total unprocessed/processed meat consumption (g/1000 kcal) was 20/5 in East Asian and 38/21 in Western participants. Unprocessed meat intakes comprised red meat for 75% in East Asian and 50% in Western participants. In Westerners, multiple linear regression analyses showed systolic/diastolic BP differences for total unprocessed red meat consumption higher by 25 g/1000 kcal +0.74/+0.57 mmHg ($P=0.03/0.01$) and for unprocessed poultry of +0.79/+0.16 mmHg ($P=0.02/0.50$). Unprocessed red meat was not related to BP in East Asian participants. In Westerners, systolic/diastolic BP differences for processed red meat higher by 12.5 g/1000 kcal were +1.20/+0.24 mmHg ($P<0.01/0.24$), due to consumption of cold cuts and sausages (+1.59/+0.32 mmHg, $P<0.001/0.27$).

Conclusion: These findings are consistent with recommendations to limit meat intake (processed and unprocessed) to maintain and improve cardiovascular health.

Introduction

The population-based INTERnational collaborative study of MAcronutrients, micronutrients and blood Pressure (INTERMAP) has previously found direct associations of red meat [1] and animal protein [2] intake with systolic blood pressure (BP). Findings from recent prospective cohort studies suggest that relationships of red meat consumption with risk of incident cardiovascular diseases (CVD) depend on whether or not the meat is processed: strong direct associations of processed red meat with CVD, but modest positive or no associations for unprocessed red meat [3-5]. Nutritional differences prevail across types of unprocessed meat (e.g., in fatty acid, cholesterol, and heme iron); processing adds significant levels of sodium and other chemical preservatives that may increase CVD risk [3, 5]. Evidence is limited on the impact of processing on the association between meat consumption and BP. Data from cross-sectional [6] and prospective [7-9] studies in Western populations showed direct associations of processed red meat with BP [6], 4-year BP change [7], and incident hypertension [9], but attenuated significant associations of unprocessed red meat with BP with adjustment for body mass index (BMI) [6, 8, 9]. Here, we investigated cross-sectional associations with BP of unprocessed and processed meat consumption, total and by type, among 4,680 adults from 17 population samples in China, Japan, the United Kingdom, and the United States using high-quality data from 8 BP readings, four multi-pass 24-hr dietary-recalls, and two timed 24-hr urine collections.

Methods

Population

The cross-sectional INTERnational Study on MAcro/micronutrients and blood Pressure (INTERMAP) surveyed 4,680 men and women ages 40 to 59 years from 17 population samples in Japan, the People’s Republic of China, the United Kingdom and the United

States [10]. Participants were randomly selected from community and workforce populations, stratified by age and sex. The average participation rate was 49%, varying from 22% in the United Kingdom to 83% in the People's Republic of China. The measurements were conducted between 1996 and 1999 during four study visits, two on consecutive days and two on consecutive days on average three weeks later. Quality control of nondietary [10] and dietary [11] data was extensive, with local, national, and international checks on completeness and integrity. Institutional ethics committee approval was obtained for each site; all participants gave written informed consent.

Of 4,895 participants initially surveyed, we excluded individuals who did not attend all four visits (**Figure S1**; *n*=110), whose dietary data were unreliable (*n*=7), with a total energy intake from any 24-h recall of <500 or >5,000 kcal/d for women and <500 or >8,000 kcal/d for men (*n*=37 total), with unavailable urine samples, with other incomplete or missing data or indication of protocol violation (*n*=61). This resulted in a study population of 4,680 participants (2,359 men and 2,321 women).

BP measurements

Systolic and diastolic BP (first and fifth Korotkoff sounds) were measured by trained staff with a random-zero sphygmomanometer. A standard range of three cuff sizes was available (standard adult, large adult, and small adult/child). BP was measured twice at each study visit, for a total of 8 measurements. Measurements were carried out on the right arm with the participant seated, after a rest of ≥5 minutes in a quiet room, with bladder empty, arm at heart level, and no physical activity, eating, drinking, or smoking in the preceding half hour.

Dietary assessment

At each visit, a trained interviewer conducted an in-depth multipass 24-hr dietary recall with extensive quality control [11]. Consumption of all foods, beverages, and supplements in the prior 24 hours was ascertained. Country-specific aids, such as food pictures, various types and sizes of containers, and fresh foods of standardised portion size were used to increase accuracy. In the United States, data were entered directly into a computer database (Nutrition Data System, version 2.91; University of Minnesota). In other countries, data were entered onto standardized forms, coded, and computerized. Nutrient intakes were calculated using country-specific food composition tables, standardized across countries by the Nutrition Coordinating Center, University of Minnesota [11, 12].

Two timed 24-hr urine specimens were obtained from each individual at the second and fourth study visit respectively. Urine aliquots were sent to a Central Laboratory, Leuven, Belgium, for electrolyte analysis; 8% of the specimens were split locally and sent blind to estimate technical error [10]. In the total population, Pearson partial correlation coefficients, adjusted for sample and sex, between reported intakes by 24-h recall and 24-hr urinary excretions were 0.51 for total protein intake and urinary urea, 0.42 for sodium, 0.55 for potassium, and 0.42 for the sodium to potassium ratio [11].

Definition of meat consumption

Total meat consumption comprised all reported meats including meat from mixed dishes. Meat was categorized in three ways [13, 14] by: 1) Processing status (unprocessed or processed) regardless of type of meat. Unprocessed meat was fresh or frozen with no other preservation method. Processed meat had undergone preservation, e.g., salting (with and without nitrates), smoking, marinating, air drying, heating during manufacture, fermentation, addition of other preservatives [13]. 2) Type of meat (unprocessed or processed red meat or poultry). 3) Type of processed red meat: fresh processed (ready-made, salted, and/or spiced, no curing), bacon, ham (cooked or cured), cold cuts and sausages, and canned meat products. The UK dietary data contained several aggregated ready-made mixed dishes with meat; intake of meat was calculated by assigning the proportion of meat, obtained from manufacturers or recipes [15].

Other lifestyle factors

Measurements were previously described by Stamler et al. [10] Height and weight were measured four times in total at first and third visits without shoes or heavy clothing; BMI (kg/m^2) was calculated. Urinary sodium and potassium were measured by emission flame photometry from two timed 24-h urine specimens obtained from all INTERMAP participants at the Central Laboratory, Leuven, Belgium. During two visits, interviewer-assisted questionnaires were used to obtain data on demographic, lifestyle factors, and disease history including alcohol intake over the preceding 7 days (mean alcohol intake over 14 days, g/24-h used in all analyses), usual hours per day of physical activity by level (sedentary, slight, moderate, heavy), leisure- or work-related physical activity (a lot, moderate, little, none), adherence to a special diet (e.g., energy restricted diet for the purpose of weight reduction) at the time of the study, and self-reported medication use. Diabetes was defined as self-reported diagnosis by physician and/or use of diabetes medication. Use of antihypertensive, cardiovascular disease or diabetes medication was defined as use of one of the following medications at either visit: ace inhibitor, antianginal, beta or calcium channel blocker, diuretics, or vasodilators.

Statistical methods

Data analyses were performed using SAS version 9.3 (SAS Institute Inc). Measurements per individual were averaged across the four visits for energy-adjusted dietary variables (g/1000 kcal) and BP, and across the two 24-hr urinary collections. Partial correlation coefficients adjusted for sample, age, and sex, pooled across East Asian and Western populations and weighted by sample size were calculated to examine associations of meat consumption with nutrient intakes and urinary electrolyte excretions. Processed meat consumption, negligible in East Asian participants, was analysed relative to BP only for Western participants. For unprocessed and processed meat separately, weighted average nutritional compositions (per 100 g) by country were calculated using data from country-specific food composition tables. The average sum of nutrients from included food items per meat category was divided by total amount consumed and converted to amount/100 g.

From the means of the first and second pairs of visits, we estimated the reliability of meat consumption for individuals using the following formula: 1/[1+(ratio/2)] x 100, where the ratio is within-participant divided by between-participant variance [16, 17]. This gives an indication of the effect of day-to-day variability on the associations with BP.

We used multivariable linear regression analyses to examine associations between meat consumption and BP; models were fitted by country, and coefficients were pooled, weighted by inverse of their variance [16, 17]. Meat categories were analysed in units of 25 g/1000 kcal corresponding to ~1SD of intake; types of processed red meat by 12.5 g/1000 kcal (~2SD). Cross-country heterogeneity of the regression coefficients was assessed by chi-square test. Although no heterogeneity was detected, results are presented for East Asian and Western participants separately because of significant diversity in dietary pattern and metabolic phenotypes [18]. Three models were used, adjusted extensively for lifestyle, medical, and dietary factors. Additionally, we investigated the influence of BMI and urinary sodium excretion on the association.

The analyses were repeated for 3 subcohorts excluding participants with medical conditions that might bias relations between meat intake and BP: 1) a subcohort excluding participants with self-reported diagnosis of hypertension and users of anti-hypertensive drugs, 2) a subcohort of nonhypertensive participants (excluding from the foregoing cohort those with high systolic BP (≥140 mmHg) or diastolic BP (≥90 mmHg), but not diagnosed with hypertension and 3) a subcohort free of major chronic disease (excluding those with prevalent cardiovascular diseases and diabetes). Stratified analyses were performed by gender and tertiles of BMI and urinary sodium to potassium excretion ratio. Inclusion of interaction terms and stratified analyses showed no evidence for potential effect modification by age, sex, smoking, or BMI. Two-tailed probability values <0.05 were considered statistically significant. To exclude the possibility of false-positive findings with multiple analyses by types of processed red meat, we applied a Bonferroni threshold of $P \leq 0.01$ ($P \leq 0.05/4$).

Results

Descriptive statistics

Mean systolic/diastolic BP was 118.9/73.5 mmHg in East-Asian participants and 118.9/74.1 mmHg in Western participants. Average daily total unprocessed meat consumption (g/1000 kcal) was 38 in Western and 20 in East Asian participants. Of total unprocessed meat, red meat contributed 50% in Western participants and 75% in East Asian participants. Of total processed meat, red meat contributes 85% comprising fresh processed red meat e.g., ready-made ham or beef burgers, kebabs (40%), cold cuts and sausages e.g., hot dogs, pork sausages, salami (25%), ham (18%), and bacon (9%).

Higher meat consumers were more often men (**Table 1**). In East Asian participants, higher meat consumers were more educated, more likely to consume alcohol, and had an unhealthier dietary pattern compared to lower meat consumers. In Western participants, higher meat consumers were more likely to smoke, had higher BMI, reported more often a history of CVD, and had unhealthier dietary patterns than those with lower meat intakes.

Reliability estimates for total unprocessed meat consumption (g/d) were 54% for the total population and 43% for total processed meat in Western participants. This implies that true associations with other variables may be larger than observed associations, e.g., 1.85 (1/0.54) times those for unprocessed meat in the total population. BP reliability estimates were 91% for systolic and 90% for diastolic BP.

Partial correlations between meat consumption and daily nutrient intakes

Unprocessed red meat intake was positively correlated with intakes of animal protein, saturated- and mono-unsaturated fatty acids, cholesterol, inversely correlated with vegetable protein and total carbohydrates, but was not correlated with urinary sodium excretion (**Table S1**). Processed meat intake was positively correlated with urinary sodium excretion. No intercorrelations were found between unprocessed and processed red meat intakes or unprocessed red meat and unprocessed poultry.

Nutritional composition of meats

Country-specific weighted average nutritional composition was calculated per 100 g of unprocessed red meat and processed red meat (**Table 2**). For the UK and US, unprocessed and processed red meats were comparable in content of energy, animal protein, heme iron, and fatty acids. Compared to unprocessed red meat, processed red meat contained 6 times higher amounts of dietary sodium in the UK and 12 times higher in the US. Dietary sodium from processed red meat contributed 13% to total sodium intake in UK and 7% to total dietary sodium intake in US participants.

Associations of unprocessed meat consumption and BP

In the total population, BP differences for total unprocessed meat consumption higher by 25 g/1000 kcal were +0.69 mmHg systolic (**Table 3:** 95%CI: 0.25, 1.14) and +0.42 mmHg diastolic (95%CI: 0.12, 0.72). This reflected significant positive associations of unprocessed red meat with systolic and diastolic BP in Western participants. Significant associations were attenuated with adjustment for BMI and prevailed with adjustment for urinary sodium excretion. Unprocessed red meat was not related to BP in East Asian participants. Sensitivity analyses for the three subcohorts excluding participants with medical conditions that might bias associations between meat intake and BP showed similar significant positive associations between unprocessed red meat consumption and BP (**Table S2**). Stratified analyses showed positive associations of unprocessed red meat with systolic BP in Western women (**Table S3:** +1.25 mmHg, 95% CI: 0.27,2.23), overweight Western participants (Table S4: +1.64 mmHg, 95% CI: 0.45,2.83), and in

Western participants in the highest tertile of urinary sodium to potassium ratio (Table S5: +1.08 mmHg, 95% CI: -0.08,2.25); and with diastolic BP in Western women (**Table S3:** +1.27 mmHg, 95% CI: 0.63,1.92).

Associations of processed meat consumption and BP in Western participants

In Western participants, total processed meat consumption higher by 25 g/1000 kcal was associated with a systolic BP difference of +1.23 mmHg (**Table 4:** 95%CI: 0.48, 1.99). A similar association with systolic BP was found for processed red meat intake (+1.20 mmHg, 95%CI: 0.37, 2.03). Significant associations attenuated with adjustment for BMI and prevailed with adjustment for urinary sodium excretion. No significant associations were found between processed meat and diastolic BP.

For individual types of processed red meat, applying a Bonferroni threshold of $P \leq 0.01$, intakes higher by 12.5 g/1000 kcal of cold cuts and sausages (+1.59 mmHg, 95%CI: 0.75, 2.43) and fresh processed red meat (+0.75 mmHg, 95%CI: 0.11, 1.39) were significantly associated with systolic BP. Only the significant association between cold cuts and sausages and systolic BP remained significant with adjustment for BMI and urinary sodium excretion.

Sensitivity analyses for the three subcohorts excluding participants with medical conditions that might bias associations showed weaker but significant associations between processed red meat consumption and systolic BP (**Table S2**). Stratified analyses in Western participants only showed significant direct associations of processed red meat with systolic BP in women (**Table S3:** +1.35 mmHg, 95%CI: 0.05,2.64), those overweight (**Table S4:** +1.69 mmHg, 95%CI: 0.20, 3.17), and those in the highest tertile of urinary sodium to potassium ratio (**Table S5:** +1.53 mmHg, 95%CI: 0.10, 2.95).

Discussion

In Western participants, our main findings were significant direct associations of unprocessed meat (red meat and/or poultry) with BP. These associations attenuated with adjustment for BMI, but prevailed with urinary sodium excretion. Processed (red) meat consumption was directly associated with systolic BP; explained by significant direct associations with specifically fresh processed red meat and cold cuts and sausages. The association of cold cuts and sausages with systolic BP remained significant with adjustment for BMI and urinary sodium excretion. In East Asian participants, direct associations were found for total unprocessed meat intake and diastolic BP. Given the cross-sectional nature of these data and the scarcity of findings from other studies, causal inferences are premature.

In Western populations, the significant associations of unprocessed red meat and BP and attenuation of adjustment for BMI were consistent with findings from one cross-sectional study of BP [6] and two prospective studies of incident hypertension [8, 9], all in European women. Although interaction by gender was not evident, stratified analyses showed significant direct associations in Western women only. Other risk factors than higher unprocessed meat intakes may contribute to a higher extent to adverse BP in men than in women.

To our knowledge, no previous studies have published associations of unprocessed red meat with BP in East Asian populations. With moderate intakes compared to Western participants, unprocessed (red) meat was not associated with systolic BP. In East Asian participants, a direct association with diastolic BP however was found for total unprocessed meat, but not for unprocessed red meat. Unprocessed poultry intake was however too low for proper analyses and warrants further research. Overall, these findings suggest that limiting meat intakes may help to maintain healthy BP.

In Western participants we did find significant direct associations with BP of unprocessed poultry intake. Previous cross-sectional [6] and prospective cohort studies [7, 8, 19, 20] showed inconsistent findings of total poultry intake with BP [6], change of BP [7, 19], and risk of hypertension [8, 20], but did not distinguish unprocessed from processed poultry. The nutritional composition of poultry depends highly by processing and especially preparation method e.g. frying and needs to be taken into account in future studies.

For processed red meat, previous cross-sectional [6] and prospective [7-9] studies observed persistent significant direct associations with systolic and diastolic BP [6], four-year BP changes [7], and incident hypertension [9] with adjustment for BMI in Western women. We found attenuated positive associations of processed red meat with systolic BP in Western populations with control for BMI, suggesting a significant contribution of BMI to this direct association. The initial direct association of processed red meat with diastolic BP was attenuated after adjustment of lifestyle factors, BMI, and urinary sodium. Other risk factors may have greater influence on adverse diastolic BP then processed red meat. These discrepancies may also be explained by methodological issues including higher validity of four 24-hr dietary recalls, eight BP, and four anthropometric measurements in the present study, with results of others were based on food frequency questionnaires [6-9], two BP measurements [6] or self-reported incidence of hypertension [7-9]. Especially intakes of fresh processed red meat (mainly hamburgers) and cold cuts and sausages (sausages, hot dogs, and salami) were directly associated with systolic BP. The higher contents of preservatives including salt or co-consumption of other unhealthy foods e.g. fries may have influenced these associations.

Our findings are difficult to compare with results of other studies on types of processed red meat intake and BP; two prospective cohort studies showed direct associations to incident hypertension with various types of processed meat [8], or only with ham but not other types [9]. Difficulties include the limited number of studies, varying definitions of processed meats, varying contributions of individual meats to types of processed meats among populations, differences in nutritional composition between types of processed meat, use of varied dietary assessment methods, and misclassification of dietary data.

The results of sensitivity analyses showed that significant findings of unprocessed and processed red meat with BP persisted after exclusion of participants with medical conditions that might bias associations between meat intake and BP. The attenuation of significant findings with adjustment for BMI and significant positive associations mainly found in overweight participants was expected due to the high intercorrelation of BMI with BP [21]. Although significant associations between unprocessed and processed meat with BP prevailed with adjustment for urinary sodium excretion, stratified analyses showed significant findings only in those in the highest tertile of sodium to potassium excretion ratio without indication of effect modification. Although lower sample sizes may have reduced the power of the analyses, these findings suggest that maintenance of BP through lower meat intakes may especially be of importance in overweight people with unhealthier lifestyles.

The average weighted nutritional composition of 100 g unprocessed or processed red meats was comparable for energy, animal protein, fatty acids, and heme iron. INTERMAP previously showed unfavourable associations with BP of total red meat [1] and animal protein [2], and positive non-significant associations of BP with heme iron [1] intakes. In contrast to unprocessed red meat intake, processed red meat intake was also correlated with urinary sodium excretion. In the US, the sodium content of processed red meat was 12-fold higher compared to unprocessed red meat. Evidence is well-established on the etiological relationship between sodium intake and BP. A meta-analysis including 37 randomised controlled trials showed for sodium intake of $<2{,}000$ mg/d versus $\geq 2{,}000$ mg/d a reduction in systolic BP of 3.47 mmHg and in diastolic BP of 1.81 mmHg [22], contributing to a lower risk of cardiovascular diseases [22, 23]. The stronger direct association observed for processed meat with BP may be due to higher sodium content.

The significant associations with BP however prevailed for unprocessed and processed red meat consumption with adjustment for urinary sodium excretion, suggesting that the unfavourable associations of unprocessed and processed meats with BP may be explained by addition of chemical preservatives [5] and combined, synergistic effects of various components in their natural food matrix [24].

Findings here are for participants from randomly selected population samples and data were collected using standardized, quality-controlled repeated methods [11]. Self-reported dietary data relies on accurate recall with typical underreport of e.g. portion sizes and condiment or overreport of healthy food intakes that may have led to recall and reporting bias. Causality cannot be definitely inferred due to the cross-sectional study design. Despite comprehensive adjustment for lifestyle and dietary confounders, the possibility of residual confounding by e.g. imprecise measurement of physical activity or unmeasured confounding factors including food availability and accessibility especially in Asia cannot be excluded. However, the direct associations of processed meat with systolic BP found in both men and women argues against potential residual confounding. Extensive adjustments including for BMI may have attenuated true associations towards the null, there was however no indication for effect modification by BMI. East Asian participants had negligible intakes of unprocessed poultry and processed meat precluding extensive analyses with BP.

Data on differential associations of unprocessed and processed meats with BP are limited. The INTERMAP findings reported here showed not only significant direct associations with BP of processed red meat consumption, mainly for consumption of cold cuts and sausages, in Western participants, but also for unprocessed meat (red meat and/or poultry). The null findings with BP of East Asian participants with moderate intakes of unprocessed meat underline potential cardiovascular benefits of limiting meat intakes. These findings emphasize and strengthen population-wide recommendations to limit meat intake (processed and unprocessed) to maintain and enhance cardiovascular health.

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Authors contributions:

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Table 1. Characteristics of INTERMAP Participants, East Asian and Western, Dichotomized by Median of Energy-adjusted Total Meat Consumption[1,2]

	East Asian participants		Western participants	
	Lower (*n*=992)	Higher (*n*=992)	Lower (*n*=1,348)	Higher (*n*=1,348)
Total meat consumption, g/1000 kcal	9±7	40±17	37±15	82±22
Age (y)	49.8±5.6	48.6±5.3	49.0±5.4	49.3±5.5
Men (%)	45.4	54.4	46.8	54.8
Education (y)	8.0±4.1	10.4±3.7	14.9±3.3	14.2±3.1
Current smokers (%)	33.5	32.2	13.7	20.1
Alcohol intake (g/d)	10.5±21.6	16.5±22.9	8.0±14.5	8.8±15.8
Physically active during leisure time (%)[3]	49.4	62.4	64.1	55.8
Moderate/heavy physical activity during work and leisure time (hr/d)	4.1±3.9	3.9±4.1	3.0±3.0	3.1±3.1
Taking dietary supplements (%)	12.6	17.9	53.3	44.8
BMI (kg/m^2)	23.4±3.3	23.2±2.9	27.6±5.3	29.7±6.0
Systolic BP (mmHg)	119.8±16.8	118.1±14.2	117.2±14.1	120.7±13.7

Diastolic BP (mmHg)	73.4±10.5	73.5±10.0	73.6±10.0	74.7±9.6
History of cardiovascular disease or diabetes mellitus (%)	9.4	9.8	12.9	16.5
Use of medication for hypertension, cardiovascular disease, or diabetes (%)	8.7	6.6	17.7	26.7
Family history of hypertension (%)				
Yes	42.5	40.7	62.8	65.7
Unknown	27.0	32.9	26.6	23.7
Adherence to any special diet (%)	7.0	5.2	18.3	19.4
Urinary sodium (mmol/24-hr)	228±87	193±66	152±54	167±61
Urinary potassium (mmol/24-hr)	43±15	46±14	61±22	58±21
Urinary sodium to potassium excretion ratio	5.9±2.7	4.5±1.8	2.7±1.1	3.1±1.3
Total energy intake (kcal/d)	2012±531	2063±481	2242±669	2218±705
Dietary consumption				
Unprocessed and processed meat (g/1000 kcal)				
Unprocessed meat	8±7	32±18	22±14	55±25
Unprocessed red meat	6±6	24±18	9±11	28±22
Unprocessed poultry	2±3	9±10	12±12	27±22

Processed meat	2±3	8±10	15±12	27±19
Processed red meat	1±3	6±8	12±11	23±18
Processed poultry	0.03±0.4	0.4±3	2±5	3±8
Types of processed red meat (g/1000 kcal)				
Fresh processed red meat	0.1±1	0.6±3	5±8	9±12
Cold cuts and sausages	0.3±1	2±4	3±5	6±9
Ham	0.5±2	2±4	2±5	4±8
Bacon	0.1±1	0.5±2	1±3	2±5
Canned red meat	0±0	0±0	0.4±2	1±4
Other red meat	0.1±1	0.3±2	0.6±2	1±5
Other food groups (g/1000 kcal)				
Raw fruit	66±66	57±56	60±70	45±61
Low-fat dairy products	6±20	8±21	59±93	37±72
Raw and cooked vegetables	149±79	146±66	81±59	81±54
Fibre-rich grain products	82±161	23±77	20±25	14±19
Fish and shellfish	27±34	37±28	11±17	9±14
Nutrient intakes				

Total protein (%kcal)	13±3	16±2	14±3	17±3
Animal protein (%kcal)	4±4	8 ±3	8±3	12±3
Total fatty acids (%kcal)	20±6	25±5	32±7	34±7
Total mono-unsaturated fatty acids (%kcal)	8±2	10±2	11±3	13±3
Total saturated fatty acids (%kcal)	5±2	7±2	11±3	11±3
Total poly-unsaturated fatty acids (%kcal)	6±2	6±2	7±2	7±2
Total trans fatty acids (%kcal)	0.3±0.4	0.3±0.4	2±1	2±1
Cholesterol (mg/1000 kcal)	126±99	177±78	110±50	149±58
Total iron (mg/1000 kcal)	7±2	6±2	8±3	7±2

[1]Participants were classified according to lower or higher total meat consumption by median intake; 22.2 g/1000 kcal in East Asian participants, 56.7 g/1000 kcal in Western participants.

[2]Mean±SD (all such values).

[3]Defined as engagement in moderate or heavy physical activity during leisure time.

Table 2. Country-specific Weighted Average Nutritional Composition per 100 g Unprocessed and Processed Red Meat[1]

	Unprocessed red meat				Processed red meat	
	Japan	China	UK	US	UK	US
Energy, kcal	254	292	198	243	238	289
Animal protein, g	22	20	21	28	19	22
Total fatty acids, g	17	23	11	14	16	21
MUFA, g	7	10	4	6	6	10
SFA, g	6	9	4	5	6	8
PUFA, g	1	3	1	1	2	1
Trans, g	0.3	0.2	0.3	0.4	0.2	0.7
Cholesterol, mg	79	146	71	100	60	80
Heme iron, mg	2.0	3.1	1.7	2.2	1.3	1.8
Sodium, mg	115	98	198	55	1198	659

[1]For unprocessed and processed meat separately, the average sum of nutrients coming from included food items was calculated using data from country-specific food composition tables, divided by consumed amount, and converted to amount per 100 g.

Table 3. Estimated Mean Difference in BP Associated With Consumption of Unprocessed Total Meat, Red Meat, and Poultry per 25 g/1000 Kcal

	Systolic BP			Diastolic BP		
	Difference	95%CI	*P*	Difference	95%CI	*P*
Total unprocessed meat						
Total population (n=4,680)						
Model 1[1]	1.00	(0.55,1.45)	<0.0001	0.61	(0.31,0.91)	<0.0001
Model 2[2]	0.67	(0.24,1.10)	<0.01	0.44	(0.14,0.73)	<0.01
Model 3[3]	0.69	(0.25,1.14)	<0.01	0.42	(0.12,0.72)	<0.01
Model 4[4]	0.33	(-0.10,0.76)	0.13	0.21	(-0.08,0.51)	0.16
Model 5[5]	0.65	(0.21,1.10)	<0.01	0.41	(0.11,0.71)	<0.01
East Asian participants (n=1,984)						
Model 1[1]	0.91	(-0.11,1.92)	0.08	0.89	(0.24,1.53)	<0.01
Model 2[2]	0.61	(-0.37,1.56)	0.21	0.73	(0.12,1.35)	0.02
Model 3[3]	0.54	(-0.43,1.50)	0.28	0.68	(0.05,1.31)	0.03
Model 4[4]	0.26	(-0.68,1.20)	0.59	0.46	(-0.15,1.07)	0.14
Model 5[5]	0.05	(-0.42,1.51)	0.27	0.69	(0.06,1.32)	0.03
Western participants (*n*=2,696)						
Model 1[1]	1.03	(0.52,1.53)	<0.0001	0.54	(0.20,0.88)	<0.01
Model 2[2]	0.68	(0.20,1.17)	<0.01	0.35	(0.02,0.68)	0.04
Model 3[3]	0.73	(0.24,1.23)	<0.01	0.35	(0.01,0.69)	0.05
Model 4[4]	0.35	(-0.14,0.83)	0.16	0.14	(-0.20,0.47)	0.43
Model 5[5]	0.68	(0.18,1.18)	<0.01	0.32	(-0.02,0.67)	0.06
Unprocessed red meat						
Total population (*n*=4,680)						
Model 1[1]	0.94	(0.36,1.52)	<0.01	0.77	(0.39,1.15)	<0.0001

Model 2[2]	0.53	(-0.02,1.09)	0.06	0.56	(0.19,0.93)	<0.01
Model 3[3]	0.52	(-0.04,1.08)	0.07	0.51	(0.14,0.89)	<0.01
Model 4[4]	0.15	(-0.39,0.70)	0.59	0.29	(-0.08,0.66)	0.12
Model 5[5]	0.49	(-0.07,1.05)	0.09	0.50	(0.12,0.88)	<0.01
East Asian participants (*n*=1,984)						
Model 1[1]	0.49	(-0.64,1.62)	0.40	0.81	(0.36,1.26)	0.06
Model 2[2]	0.07	(-0.98,1.13)	0.89	0.47	(-0.22,1.15)	0.18
Model 3[3]	-0.06	(-1.14,1.01)	0.91	0.37	(-0.32,1.07)	0.29
Model 4[4]	-0.26	(-1.31,0.78)	0.62	0.19	(-0.48,0.86)	0.58
Model 5[5]	-0.06	(-1.14,1.01)	0.91	0.37	(-0.32,1.07)	0.29
Western participants (*n*=2,696)						
Model 1[1]	1.10	(0.43,1.77)	<0.01	0.81	(0.36,1.26)	<0.001
Model 2[2]	0.71	(0.06,1.35)	0.03	0.60	(0.16,1.05)	<0.01
Model 3[3]	0.74	(0.09,1.40)	0.03	0.57	(0.12,1.02)	0.01
Model 4[4]	0.31	(-0.33,0.95)	0.35	0.34	(-0.11,0.78)	0.14
Model 5[5]	0.70	(0.04,1.35)	0.04	0.55	(0.10,1.00)	0.02
Unprocessed poultry						
Western participants (*n*=2,696)						
Model 1[1]	0.79	(0.11,1.47)	0.02	0.18	(-0.28,0.64)	0.44
Model 2[2]	0.56	(-0.09,1.21)	0.09	0.05	(-0.39,0.50)	0.81
Model 3[3]	0.79	(0.12,1.45)	0.02	0.16	(-0.30,0.61)	0.50
Model 4[4]	0.45	(-0.19,1.10)	0.17	-0.03	(-0.48,0.42)	0.89
Model 5[5]	0.73	(0.07,1.40)	0.03	0.13	(-0.32,0.59)	0.56

[1]Model 1 was adjusted for age, sex, and sample.

[2]Model 2 was adjusted as model 1 plus intakes of energy (kcal) and alcohol (g/d), smoking status (never, former, current), years of education (years completed), physical activity

during leisure time (a lot, moderate, little, none), use of dietary supplements (yes/no), adherence to any special diet (yes/no), history of cardiovascular disease or diabetes mellitus (yes/no), family history of cardiovascular disease (yes/no), use of antihypertensive, cardiovascular disease or diabetes medication (yes/no).

[3]Model 3 was adjusted as model 2 plus intakes (g/1000 kcal) of low-fat dairy products, raw fruits, raw and cooked vegetables, fiber-rich cereals and grains, fish and shell fish, and mutually for the sum of intakes of other meat types.

[4]Model 4 was adjusted as model 3 plus BMI.

[5]Model 5 was adjusted as model 3 plus 24-hr urinary sodium excretion.

Table 4. Estimated Mean Difference in BP Associated With Consumption of Processed Meat, Processed Red Meat and its Types in Western Participants (n=2,696)

	Systolic BP			Diastolic BP		
	Difference	95%CI	*P*	Difference	95%CI	*P*
Total processed meat (per 25 g/1000 kcal)						
Model 1[1]	1.94	(1.19,2.70)	<0.0001	0.71	(0.20,1.22)	<0.01
Model 2[2]	1.18	(0.44,1.92)	<0.01	0.36	(-0.14,0.87)	0.16
Model 3[3]	1.23	(0.48,1.99)	<0.01	0.36	(-0.16,0.88)	0.17
Model 4[4]	0.57	(-0.17,1.31)	0.13	-0.01	(-0.52,0.51)	0.98
Model 5[5]	1.04	(0.27,1.81)	<0.01	0.27	(-0.26,0.80)	0.31
Processed red meat (per 25 g/1000 kcal)						
Model 1[1]	2.02	(1.19,2.85)	<0.0001	0.74	(0.17,1.30)	0.01
Model 2[2]	1.22	(0.41,2.03)	<0.01	0.38	(-0.18,0.94)	0.18
Model 3[3]	1.20	(0.37,2.03)	<0.01	0.34	(-0.23,0.92)	0.24
Model 4[4]	0.51	(-0.30,1.33)	0.22	-0.04	(-0.61,0.53)	0.89
Model 5[5]	1.03	(0.18,1.87)	0.02	0.26	(-0.32,0.84)	0.38
Fresh processed red meat (per 12.5 g/1000 kcal)[6]						
Model 1[1]	1.09	(0.44,1.74)	<0.01	0.45	(0.00,0.89)	0.05
Model 2[2]	0.61	(-0.01,1.24)	0.05	0.27	(-0.16,0.70)	0.21
Model 3[3]	0.75	(0.11,1.39)	0.02	0.29	(-0.15,0.73)	0.20
Model 4[4]	0.44	(-0.18,1.06)	0.17	0.11	(-0.32,0.54)	0.61
Model 5[5]	0.71	(0.07,1.35)	0.03	0.27	(-0.17,0.71)	0.23
Bacon (per 12.5 g/1000 kcal)[6]						
Model 1[1]	1.37	(-0.29,3.03)	0.11	0.44	(-0.67,1.55)	0.44
Model 2[2]	0.54	(-1.07,2.16)	0.51	0.02	(-1.08,1.11)	0.98
Model 3[3]	0.22	(-1.41,1.85)	0.79	0.04	(-1.06,1.15)	0.94
Model 4[4]	0.04	(-1.53,1.61)	0.96	-0.06	(-1.14,1.03)	0.92

Model 5[5]	0.07	(-1.58,1.73)	0.93	-0.04	(-1.16,1.08)	0.95
Cold cuts and sausages (per 12.5 g/1000 kcal)[6]						
Model 1[1]	2.17	(1.32,3.03)	<0.0001	0.62	(0.04,1.20)	0.04
Model 2[2]	1.71	(0.88,2.54)	<0.001	0.42	(-0.15,0.99)	0.15
Model 3[3]	1.59	(0.75,2.43)	<0.001	0.32	(-0.25,0.90)	0.27
Model 4[4]	1.03	(0.21,1.84)	0.01	0.01	(-0.56,0.58)	0.97
Model 5[5]	1.45	(0.61,2.30)	<0.01	0.26	(-0.32,0.84)	0.38
Ham (per 12.5 g/1000 kcal)[6]						
Model 1[1]	-0.62	(-1.56,0.32)	0.20	-0.20	(-0.83,0.44)	0.54
Model 2[2]	-0.85	(-1.74,0.05)	0.06	-0.31	(-0.93,0.30)	0.32
Model 3[3]	-0.82	(-1.71,0.07)	0.07	-0.31	(-0.92,0.30)	0.32
Model 4[4]	-1.04	(-1.91,-0.18)	0.02	-0.43	(-1.03,0.17)	0.16
Model 5[5]	-0.94	(-1.84,-0.05)	0.04	-0.36	(-0.98,0.25)	0.25

[1]Model 1 was adjusted for age, sex, and sample.

[2]Model 2 was adjusted as model 1 plus intakes of energy (kcal) and alcohol (g/d), smoking status (never, former, current), years of education (years completed), physical activity during leisure time (a lot, moderate, little, none), use of dietary supplements (yes/no), adherence to any special diet (yes/no), history of cardiovascular disease or diabetes mellitus (yes/no), family history of cardiovascular disease (yes/no), use of antihypertensive, cardiovascular disease or diabetes medication (yes/no).

[3]Model 3 was adjusted as model 2 plus intakes (g/1000 kcal) of low-fat dairy products, raw fruits, raw and cooked vegetables, fiber-rich cereals and grains, fish and shell fish, and mutually for the sum of other meat types.

[4]Model 4 was adjusted as model 3 plus BMI.

[5]Model 5 was adjusted as model 3 plus 24-hr urinary sodium excretion.

[6]Statistical significance based on a Bonferroni threshold of $P \leq 0.01$ ($P \leq 0.05/4$).