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Animal food intake and cooking methods in relation to endometrial cancer risk in Shanghai

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We evaluated animal food intake and cooking methods in relation to endometrial cancer risk in a population-based case–control study in Shanghai, China. A validated food frequency questionnaire was used to collect the usual dietary habits of 1204 cases and 1212 controls aged 30–69 years between 1997 and 2003. Statistical analyses were based on an unconditional logistic regression model adjusting for potential confounders. High intake of meat and fish was associated with an increased risk of endometrial cancer, with adjusted odds ratios for the highest *vs* the lowest quartile groups being 1.7 (95% confidence interval: 1.3–2.2) and 2.4 (1.8–3.1), respectively. The elevated risk was observed for all types of meat and fish intake. Intake of eggs and milk was not related to risk. Cooking methods and doneness levels for meat and fish were not associated with risk, nor did they modify the association with meat and fish consumption. Our study suggests that animal food consumption may play an important role in the aetiology of endometrial cancer, but cooking methods have minimal influence on risk among Chinese women.
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Endometrial cancer, a hormone-dependent disease, has an incidence rate in developing countries, such as China, more than 10 times lower than that in developed countries (Parkin *et al*, 2003). However, established hormonal risk factors, including menopausal status, parity, oral contraceptive use, hormone replacement therapy and body mass index, can only explain part of the large international variation in its incidence (Kaaks *et al*, 2002). Ecological studies suggest that dietary habits have a major contribution to this international variation (Armstrong and Doll, 1975; Parkin, 1989). Several studies found that high consumption of red meat was associated with increased risk of endometrial cancer (Levi *et al*, 1993; Shu *et al*, 1993; Goodman *et al*, 1997), whereas others found no association (La Vecchia *et al*, 1986; Zheng *et al*, 1995; McCann *et al*, 2000; Jain *et al*, 2000). Three studies reported that high dietary intake of fish was inversely associated with risk (La Vecchia *et al*, 1986; McCann *et al*, 2000; Terry and Wolk *et al*, 2002), two found no association (Levi *et al*, 1993; Goodman *et al*, 1997), and two others observed a positive association (Shu *et al*, 1993; Zheng *et al*, 1995). Intake of eggs was related to an elevated risk in some (Levi *et al*, 1993, Zheng *et al*, 1995; Goodman *et al*, 1997; Terry and Vainio *et al*, 2002) but not in other studies (La Vecchia *et al*, 1986). On the other hand, consumption of milk was not associated with any increased risk in most studies (La Vecchia *et al*, 1986; Zheng *et al*, 1995; Goodman *et al*, 1997; Jain *et al*, 2000; McCann *et al*, 2000; Terry and Vainio *et al*, 2002) but was related to reduced risk in two studies (Barbone *et al*, 1993; Petridou *et al*, 2002). Most studies, however, have been conducted in Western countries, and none have evaluated potential interactions with cooking methods, which may partly explain the inconsistency in previous studies. *In vivo* and *in vitro* studies have suggested that meats cooked at a high temperature generate heterocyclic amines (HCAs) and other potent mutagens and carcinogens, which can induce tumours in multiple tissue sites in many animal species (Spingarn *et al*, 1980; Wakabayashi *et al*, 1992; Okochi *et al*, 1999; Nagao *et al*, 2002). Although a number of epidemiologic studies suggest a possible link between dietary intake of HCAs and risk of colorectal and breast cancers (Zheng *et al*, 1998; Nowell *et al*, 2002; Sinha *et al*, 2005), no studies have been conducted on endometrial cancer.

In a large case–control study, we investigated whether dietary intake of animal foods is associated with endometrial cancer risk and whether this is modified by cooking methods.

SUBJECTS AND METHODS

Eligible cases for the study were residents of urban Shanghai, aged 30–69 years, newly diagnosed with endometrial cancer between 1997 and 2003. A total of 1454 endometrial cancer cases were identified through the Shanghai Cancer Registry, and 1204 of them were interviewed, yielding a response rate of 82.8%. All cases were confirmed either by histopathology or by medical history review. Excluded from the analysis were 135 cases who refused to be interviewed (9.3%), 66 who died before interview (4.5%), 23 (1.6%) who could not be located, 12 who were out of town during the

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period of interview (0.8%), and 14 who could not be interviewed for other miscellaneous reasons (1.0%). The median interval between diagnosis and interview was 5.6 months.

Controls were randomly selected from the Shanghai Resident Registry and frequency matched to cases according to age distribution of endometrial cancer cases in 1996. After exclusion of 63 women who reported a hysterectomy, 1212 out of 1629 eligible controls (74.4%) consented and were interviewed for the study. Reasons for non-participation among controls were refusal ($n=340$, 20.9%), being out of town during the period of interview ($n=61$, 3.7%), severe illness ($n=13$, 0.8%), and other miscellaneous reasons ($n=3$, 0.2%).

Study participants were interviewed in person by trained nurses and physicians, using a structured questionnaire to obtain information on demographic characteristics, menstrual and reproductive events, exogenous hormone use, diet, cigarette smoking, alcohol consumption, physical activity, family history of cancer, and medical history. Direct body measurements on body height, weight, and waist and hip size were conducted at the time of interview. The quantitative food frequency questionnaire (FFQ) used in the study has been validated by two FFQ surveys and one 24-h diet recall survey (Shu *et al*, 2004). The FFQ listed 76 food items commonly consumed in Shanghai, including 19 animal food items which were classified into the following 10 food groups: red meat, organ meat, poultry, marine fish, fresh water fish, shrimp and crab, eel, shellfish, eggs, and milk. Red meat included pork, beef, and mutton meat. Each subject was asked to report her usual intake frequency (per day, week, month, or year) and amount in liangs (50 g) for each food item over the past 5 years, ignoring any recent changes. The participant was also asked whether she used deep-frying, stir-frying or roasting/grilling methods to prepare meats and fish, in addition to how frequently she used each cooking method in cooking these foods. The subject was also asked to report whether she usually deep-fried meat and fish to the level that (1) the surface still had a bloody colour; (2) virtually no surface was brown; (3) a small portion of the surface was brown (Goodman *et al*, 1997); the majority of the surface was brown; or (5) the entire surface was brown with a slightly burnt flavour. Levels 4 and 5 were referred to as well-done.

Consumption of common animal foods was categorised into four groups based on the quartile distribution among controls. Uncommon animal foods, such as organ meat, eel, shellfish, and milk were grouped into two levels, never and ever. The Wilcoxon rank sum test was used for comparisons of the median difference between cases and controls and the χ^2-test was used for categorical variables. An unconditional logistic regression model was applied to obtain maximum likelihood estimates of the odds ratios (ORs) and their 95% confidence intervals (CIs). All of the ORs were adjusted for age (as a continuous variable), menopausal status (pre/post menopausal), diagnosis of diabetes (ever/never), alcohol consumption (ever/never), body mass index (BMI) (as a continuous variable), physical activity in metabolic equivalent tasks (as a continuous variable), and total energy intake (as a continuous variable). Other variables, including dietary intake of total vegetables and soy foods, did not appreciably alter the risk estimates and were not adjusted for in our analyses. Tests for trend across quartiles were performed in a logistic regression model by assigning a numerical score (1–4) to each category of categorised variables. Stratified analyses were conducted to evaluate potential modifying effects.

RESULTS

Table 1 shows comparisons of cases and controls for demographic factors and known risk factors of endometrial cancer. No significant differences were observed between cases and controls for age, income, marital status, use of hormone replacement

Table 1 Comparison between cases and controls of demographics and selected risk factors in Shanghai Endometrial Cancer Study

	Cases ($n=1204$)	Controls ($n=1212$)	*P*-value
Age (Mean ± s.d.)[a]	54.5 ± 8.5	54.6 ± 8.5	0.77
Education levels (%)[b]			
No formal education	95 (8.0)	133 (11.0)	
Primary school	170 (14.1)	157 (12.9)	
Middle school	446 (37.0)	441 (36.4)	
High school	311 (25.8)	326 (27.0)	
College or above	182 (15.1)	155 (12.8)	0.05
Per capita income in previous year (yuan) (%)[b]			
<4166.67	321 (26.7)	353 (29.1)	
4166.68–6250.00	317 (26.3)	317 (26.2)	
6250.01–8750.00	261 (21.7)	267 (22.0)	
>8750.00	305 (25.3)	275 (22.7)	0.11
Marital status (%)[b]			
Unmarried	18 (1.5)	13 (1.1)	
Married or cohabiting	1055 (87.6)	1062 (87.6)	
Separated/divorced/widowed	131 (10.9)	137 (11.3)	0.63
Menopausal status (%)[b]			
No	502 (41.7)	447 (36.9)	
Yes	702 (58.3)	765 (63.1)	0.02
Age at menarche (mean ± s.d.)[a]	14.5 ± 1.7	14.8 ± 1.8	<0.01
Age at menopause (mean ± s.d.)[a]	50.2 ± 3.6	49.0 ± 3.8	<0.01
Years of menstruation (mean ± s.d.)[a]	32.8 ± 4.9	30.6 ± 5.4	<0.01
Number of pregnancies (mean ± s.d.)[a]	2.6 ± 1.5	2.9 ± 1.5	<0.01
Regularly exercise (%)[b]			
Never	859 (71.4)	806 (66.5)	
Ever	345 (28.6)	406 (33.5)	0.01
Oral contraceptive use (%)[b]			
Never	981 (81.5)	910 (75.1)	
Ever	223 (18.5)	302 (24.9)	<0.01
Any cancer history among the first-degree relatives (%)[b]			
No	774 (64.8)	867 (72.1)	
Yes	420 (35.2)	336 (27.9)	<0.01
Cigarette smoking (%)[b]			
Never	1163 (96.6)	1170 (96.5)	
Ever	41 (3.4)	42 (3.5)	0.94
Alcohol consumption (%)[b]			
Never	1170 (97.2)	1147 (94.6)	
Ever	34 (2.8)	65 (5.4)	<0.01
Body height (m) (mean ± s.d.)[a]	1.58 (0.06)	1.57 (0.05)	<0.01
Body weight (kg) (mean ± s.d.)[a]	64.0 (10.7)	58.8 (9.0)	<0.01
BMI ($kg\,m^2$) (mean ± s.d.)[a]	25.7 ± 4.1	23.8 ± 3.5	<0.01
Hormone replacement therapy (%)[b]			
Never	1151 (95.6)	1162 (96.0)	
Ever	53 (4.4)	49 (4.0)	0.66
Diabetes mellitus[b]			
Never	1009 (84.7)	1121 (93.1)	
Ever	182 (15.3)	83 (6.9)	<0.01
Total vegetable intake (mean ± s.d.)[a]	328.1 ± 205.8	325.4 ± 206.2	0.75
Total fruit intake (mean ± s.d.)[a]	225.5 ± 174.1	223.0 ± 195.4	0.75
Soy protein intake (mean ± s.d.)[a]	11.7 ± 8.4	12.0 ± 9.1	0.46
Total energy intake (mean ± s.d.)[a]	1086.5 ± 466.7	1763.5 ± 468.8	0.02

BMI = body mass index; s.d. = standard deviation. Subjects with missing values were excluded from the analysis. [a]*P*-value for *t*-test. [b]*P*-value for χ^2-test.

Epidemiology

Table 2 Intake levels of animal foods among cases and controls in Shanghai Endometrial Cancer Study

Animal foods	Median (25th, 75th percentile) Cases ($n=1204$)	Controls ($n=1212$)	*P*-value[a]
Total meat	59.7 (37.0, 89.3)	52.1 (31.2, 81.7)	<0.01
Red meat	43.7 (25.7, 67.1)	38.6 (22.4, 61.9)	<0.01
Organ meat	0.1 (0.0, 1.3)	0.0 (0.0, 1.2)	0.25
Poultry	10.9 (4.6, 22.0)	8.7 (4.0, 18.5)	<0.01
Fish, shrimp, crab, and eel	47.3 (24.6, 78.9)	35.9 (17.6, 65.7)	<0.01
Marine fish	12.1 (4.8, 26.2)	10.5 (3.6, 26.2)	<0.01
Fresh water fish	12.6 (4.8, 21.1)	9.7 (3.1, 21.1)	<0.01
Shrimp and crab	5.8 (2.9, 16.7)	4.8 (1.9, 12.5)	<0.01
Eel	0.5 (0.0, 3.5)	0.2 (0.0, 2.3)	<0.01
Shellfish	0.3 (0.0, 1.1)	0.2 (0.0, 1.1)	0.02
Eggs	25.0 (12.5, 43.7)	25.0 (12.5, 43.7)	0.56
Milk	9.9 (0.0, 25.0)	10.7 (0.0, 25.0)	0.76

[a]*P*-value: Wilcoxon rank sum test.

therapy, mean intake of vegetables, or intake of fruits and soy protein. Compared with controls, cases were more likely to have attended higher education, have an earlier age at menarche, a later age at menopause, more years of menstruation, and to be premenopausal. Cases were also more likely to be diagnosed with diabetes, have a family history of cancer, have a higher total energy intake and a higher BMI, and were less likely to have had a pregnancy, engaged in regular exercise, used oral contraceptives, or consumed alcohol regularly (Table 1).

Presented in Table 2 are comparisons of the average intake levels of total and individual animal foods between cases and controls. The median intakes of red meat, poultry, marine fish, fresh water fish, shrimp and crab, eel, and shellfish were significantly higher in cases than in controls. No significant differences were found for intake of organ meat, eggs, and milk.

The associations between animal food intake and endometrial cancer risk are presented in Table 3. The ORs were 1.7 (95% CI: 1.3–2.2) and 2.4 (95% CI: 1.8–3.1), respectively, for those who ate total meat and total fish in the highest intake quartile as compared with those in the lowest quartile. A positive association was observed for consumption of red meat, poultry, marine fish, fresh water fish, shrimp and crab. Consumption of organ meat, eel, shellfish, and milk was not very common in our study population. A moderately increased risk (OR = 1.3, 95% CI: 1.1–1.6) was found to be associated with eel or shellfish consumption. Egg and milk consumption were not associated with endometrial cancer risk. No case–control difference was found regarding ever/never eating organ meat. The consumption of organ meat in this study population was too low to evaluate disease risk by intake level.

Neither cooking method nor doneness level of meat and fish were associated with endometrial cancer risk, nor did they modify the association of meat and fish intake with disease risk (Table 4). Additional analyses stratified by consumption of total vegetables and soyfood did not show substantial changes in the above-mentioned associations (data not shown).

DISCUSSION

The positive association of disease with intake of red meat and the null association with eggs and milk found in the current study are consistent with those found in previous studies (La Vecchia *et al*, 1986; Levi *et al*, 1993; Shu *et al*, 1993; Zheng *et al*, 1995; Goodman *et al*, 1997; McCann *et al*, 2000; Jain *et al*, 2000; Terry and Vainio *et al*, 2002). However, our finding of a positive association with intake of poultry was inconsistent with previous reports in which null (Okochi *et al*, 1999; McCann *et al*, 2000) or inverse (Goodman *et al*, 1997) associations were reported. Our observation of an elevated risk associated with a high consumption of fish, although inconsistent with some previous studies (La Vecchia *et al*, 1986; Levi *et al*, 1993; Goodman *et al*, 1997; McCann *et al*, 2000; Terry and Wolk *et al*, 2002), is in line with that from our earlier report on the same disease (Shu *et al*, 1993). Endometrial cancer is a hormone-dependent disease. It has been suggested that dietary fat is responsible for the association between animal foods and endometrial cancer risk (Levi *et al*, 1993; Goodman *et al*, 1997), probably through influencing oestrogen metabolism and enhancing oestrogen re-absorption in the bowel (Gorbach and Goldin, 1987), although the relation between dietary fat and endogenous oestrogen levels remains controversial (Holmes *et al*, 2000). *In vitro* and *in vivo* studies have found that omega-3 fatty acids, which fish, particularly marine fish, are rich in, inhibit the proliferation and progression of hormone-related cancer (Ip, 1997; Rose and Connolly, 1999). On the other hand, omega-6 fatty acids were found to increase synthesis of cyclooxygenase- and lipoxygenase-catalysed products and thus may increase cancer risk (Nair *et al*, 1997). It has been shown that farm-raised fish are high in omega-6 but low in omega-3 fatty acids (van Vliet and Katan, 1990). The high consumption of fresh water fish in our study population compared to the high intake of marine fish among Western populations may explain the contradictory findings on fish consumption in our study compared to those conducted in Western countries.

Chemical pollution may be another explanation for our finding on fish. Fish growing in polluted water may have a high level of methylmercury, polychlorinated dibenzo-*p*-dioxins, dibenzofurans, organochlorine residues, and other chemicals. Some of these chemicals have high toxicity and carcinogenic potency (Rojas *et al*, 1999). Fresh-water fish have been found to be contaminated with methyl mercury, organochlorines, and other chemicals in China (Hou *et al*, 1988; Nakata *et al*, 2002). Evidence that organochlorines are present in seafood is also available (Jiang *et al*, 2005). Several studies conducted in Shanghai, including this one, have consistently found that fish intake is related to an increased risk of several cancers, including cancers of breast, endometrium, and colorectum (Shu *et al*, 1993; Guo *et al*, 1994; Dai *et al*, 2002; Chiu *et al*, 2003), suggesting that water pollution may be involved in the aetiology of these cancers. Organochlorines have been shown to have estrogenic activity (Olea *et al*, 1998; Brouwer *et al*, 1999) and may increase the risk of hormone-related cancers such as prostate and breast cancer (Terry *et al*, 2003). However, results from two studies that have directly evaluated the association between organochlorines and endometrial cancer found either no significant association (Weiderpass *et al*, 2000) or a negative association (Sturgeon *et al*, 1998). Further studies are needed to search for the factors that are responsible for the positive association between fish consumption and cancer risk in this population.

Meat and fish cooked at high temperatures can produce HCAs, potent experimental mutagens, or carcinogens (Dolara *et al*, 1979; Sinha and Knize *et al*, 1998; Sinha and Rothman *et al*, 1998; Wong *et al*, 2005). Heterocyclic amines begin to form at temperatures of 150°C or higher, and their production can be increased up to three-fold when the cooking temperature is increased from 200 to 250°C (Dolara *et al*, 1979). Frying, broiling, grilling, and baking are associated with formation of large amounts of HCAs (Sinha and Knize *et al*, 1998; Sinha and Rothman *et al*, 1998). In our population, deep-frying is the most common high-temperature method for cooking red meat and fish, whereas roasting or grilling is less common, although it may be used to cook poultry. Oil temperature is normally around 240–270°C during deep-frying. It has been reported that deep-frying also generates fumes containing mutagenic compounds (de Meester and Gerber, 1995; Shields *et al*, 1995). These mutagens or carcinogens have been linked to an

Table 3 Odds ratios and 95% CIs for animal food intake in association with endometrial cancer risk

	Quartile of intake (g day^{-1})				
Food groups	**Q1 (Low)**	**Q2**	**Q3**	**Q4 (High)**	***P*-value for trend**
Total meat intake					
Cases/controls	224/303	271/303	348/303	361/303	
OR1	1.0	1.2 (0.9–1.5)	1.5 (1.2–1.9)	1.6 (1.3–2.0)	<0.01
OR2	1.0	1.2 (0.9–1.6)	1.6 (1.3–2.1)	1.7 (1.3–2.2)	<0.01
Red meat					
Cases/controls	238/303	290/303	325/303	351/303	
OR1	1.0	1.2 (0.9–1.5)	1.4 (1.1–1.7)	1.4 (1.1–1.8)	<0.01
OR2	1.0	1.2 (0.9–1.5)	1.4 (1.1–1.8)	1.4 (1.1–1.9)	<0.01
OR3[a]	1.0	1.2 (0.9–1.5)	1.3 (1.0–1.7)	1.3 (1.0–1.8)	0.02
Organ meat					
Cases/controls	598/625 (Never)	606/587 (Ever)			
OR1	1.0	1.1 (0.9–1.3)			
OR2	1.0	1.1 (0.9–1.4)			
OR3[a]	1.0	1.1 (0.9–1.4)			
Poultry					
Cases/controls	254/303	282/335	285/272	383/302	
OR1	1.0	1.0 (0.8–1.2)	1.3 (1.0–1.6)	1.5 (1.2–1.9)	<0.01
OR2	1.0	1.0 (0.8–1.3)	1.4 (1.1–1.8)	1.6 (1.3–2.1)	<0.01
OR3[a]	1.0	1.0 (0.8–1.3)	1.4 (1.1–1.8)	1.6 (1.2–2.0)	<0.01
Total fish					
Cases/controls	183/303	291/303	317/303	413/303	
OR1	1.0	1.7 (1.3–2.1)	1.9 (1.5–2.4)	2.3 (1.8–3.0)	<0.01
OR2	1.0	1.7 (1.3–2.2)	1.9 (1.4–2.4)	2.4 (1.8–3.1)	<0.01
Marine fish					
Cases/controls	295/341	244/269	407/391	258/211	
OR1	1.0	1.0 (0.8–1.3)	1.2 (1.0–1.5)	1.4 (1.1–1.8)	<0.01
OR2	1.0	1.0 (0.8–1.3)	1.2 (0.9–1.5)	1.3 (1.0–1.7)	0.02
OR3[b]	1.0	1.0 (0.8–1.3)	1.1 (0.9–1.4)	1.2 (0.9–1.5)	0.18
Fresh water fish					
Cases/controls	217/303	305/360	391/338	291/211	
OR1	1.0	1.2 (0.9–1.5)	1.6 (1.3–2.0)	1.9 (1.5–2.4)	<0.01
OR2	1.0	1.2 (0.9–1.5)	1.6 (1.3–2.0)	1.9 (1.5–2.5)	<0.01
OR3[b]	1.0	1.2 (0.9–1.5)	1.6 (1.3–2.0)	1.9 (1.4–2.4)	<0.01
Shrimp and crab					
Cases/controls	265/320	319/294	282/326	338/272	
OR1	1.0	1.3 (1.0–1.6)	1.0 (0.8–1.3)	1.5 (1.2–1.9)	<0.01
OR2	1.0	1.4 (1.1–1.7)	1.1 (0.9–1.4)	1.6 (1.2–2.0)	0.01
OR3[b]	1.0	1.3 (1.0–1.7)	1.0 (0.8–1.3)	1.4 (1.0–1.8)	0.12
Eel					
Cases/controls	515/594 (Never)	689/618 (Ever)			
OR1	1.0	1.3 (1.1–1.5)			
OR2	1.0	1.3 (1.1–1.6)			
OR3[b]	1.0	1.3 (1.1–1.6)			
Shellfish					
Cases/controls	470/541 (Never)	734/671 (Ever)			
OR1	1.0	1.3 (1.1–1.5)			
OR2	1.0	1.3 (1.1–1.6)			
Eggs					
Cases/controls	326/356	342/303	409/401	127/152	
OR1	1.0	1.2 (1.0–1.5)	1.1 (0.9–1.4)	0.9 (0.7–1.2)	0.81
OR2	1.0	1.2 (1.0–1.6)	1.1 (0.9–1.4)	0.9 (0.7–1.2)	0.81
Milk					
Cases/controls	493/466 (Never)	711/746 (Ever)			
OR1	1.0	0.9 (0.8–1.1)			
OR2	1.0	1.0 (0.8–1.2)			

BMI = body mass index; CI = confidence interval. OR1: Adjusted for age. OR2: Adjusted for age, menopausal status, diagnosis of diabetes, alcohol consumption, BMI, physical activity, and total energy intake. [a]OR3: Additionally adjusted for meat intake other than target meat (as a continuous variable). [b]OR3: Additionally adjusted for fish intake other than target fish (as a continuous variable).

Table 4 Joint effect of meat and fish intake (g day^{-1}) with frequency of deep-frying and barbecuing and level of doneness

	Use of deep-fried and barbecue cooking method					
	Ever			Well done		
Amount of consumption in tertile groups	**Never**	**< 1 per month**	**⩾1 per month**	**Never**	**< 1 per month**	**⩾1 per month**
Red meat						
⩽27.2	193/234	99/124	37/46	193/234	91/104	35/41
	1.0	0.9 (0.7–1.3)	1.0 (0.6–1.6)	1.0	1.0 (0.7–1.3)	1.0 (0.6–1.6)
27.3–52.1	178/189	143/117	89/99	178/189	123/95	76/93
	1.1 (0.8–1.4)	1.5 (1.1–2.1)	1.1 (0.8–1.6)	1.0 (0.8–1.3)	1.5 (1.1–2.0)	0.9 (0.7–1.4)
>52.1	175/162	129/100	160/141	175/162	111/81	140/128
	1.2 (0.9–1.7)	1.5 (1.1–2.2)	1.4 (1.0–1.9)	1.1 (0.9–1.5)	1.5 (1.0–2.1)	1.2 (0.9–1.7)
P-value for interaction test		0.54			0.61	
Poultry						
⩽5.4	168/222	124/143	36/44	168/222	112/124	35/43
	1.0	1.1 (0.8–1.5)	1.2 (0.7–1.9)	1.0	1.1 (0.8–1.6)	1.1 (0.7–1.9)
5.5–13.1	130/152	128/118	119/131	130/152	116/105	116/123
	1.1 (0.8–1.6)	1.6 (1.1–2.2)	1.2 (0.9–1.7)	1.1 (0.8–1.5)	1.6 (1.1–2.2)	1.2 (0.9–1.7)
>13.1	144/117	140/95	214/190	144/117	128/81	200/178
	1.7 (1.2–2.4)	2.1 (1.5–3.0)	1.5 (1.1–2.0)	1.6 (1.2–2.3)	2.2 (1.5–3.1)	1.5 (1.1–1.9)
P-value for interaction test		0.71			0.71	
Total fish						
⩽23.9	143/241	75/113	114/110	143/241	63/93	103/100
	1.0	1.2 (0.8–1.7)	1.7 (1.2–2.5)	1.0	1.0 (0.7–1.5)	1.4 (1.0–2.0)
24.0–53.0	104/136	81/74	131/120	104/136	69/57	114/109
	1.3 (0.9–1.8)	2.0 (1.4–3.0)	1.9 (1.4–2.7)	1.1 (0.8–1.5)	1.8 (1.2–2.7)	1.5 (1.1–2.1)
>53.0	179/139	103/86	270/193	179/139	90/71	243/170
	2.3 (1.6–3.1)	2.1 (1.5–3.1)	2.5 (1.8–3.3)	1.8 (1.4–2.5)	1.8 (1.3–2.6)	2.0 (1.5–2.7)
P-value for interaction test		0.29			0.32	

BMI = body mass index; OR = odds ratio. OR: Adjusted for age, menopausal status, diagnosis of diabetes, alcohol consumption, physical activity, BMI, and total energy intake.

increased risk of cancers among Western populations (Zimmerli *et al*, 2001; Sinha *et al*, 2005). However, in our study, we found no association between cooking patterns or doneness levels and the risk of endometrial cancer, nor did they modify the risk associated with meat intake with the exception of the positive association with deep-fried cooking observed among women whose consumption of fish was in the lowest quartile. The latter is likely to be attributed to a chance finding owing to the lack of an underlying biological mechanism and the multiple comparisons conducted in this study. Our findings may reflect the fact that deep-frying, roasting, and grilling are much less common among the Chinese compared to people living in Western countries (Koh *et al*, 2005). In Shanghai, stir-frying is the most common cooking practice. Thus, the exposure to HCAs in our study population may not have been high enough to increase cancer risk.

Compared with Western populations, our study population has a much lower level of meat consumption. On average, the total meat intake is only about half to one-third of that consumed in Western countries (Sinha *et al*, 2005; Gonzalez *et al*, 2006). Our findings provide potent evidence of the unfavourable role of meat intake in the development of endometrial cancer, even at a low average level of consumption, and thus strongly support public health messages suggesting that women should be encouraged to lower their meat intake.

The strengths of our study include a population-based design, a large sample size, high response rates, and the availability of detailed dietary information collected using a validated FFQ. Given the nature of the case–control study design, however, recall bias is a major concern in our study. In this study, the response rate among controls (74.4%) is lower than that in cases (82.8%), raising a concern about selective participation bias. Although neither the potential study participants nor the interviewers knew our study hypotheses, we cannot exclude the possibility that study participation would be influenced by general health knowledge including healthy dietary habits. However, we found that the controls of the current study had patterns of meat and fish intake similar to the controls of the Shanghai Breast Cancer Study which was conducted in the same population 2–3 years before the current study which had a much higher response rate (91.1% for cases and 90.3% for controls) (Dai *et al*, 2002). Therefore, selection bias is unlikely to be the main explanation for the study findings. The dietary intake of cases may have changed as a result of cancer diagnosis and treatment, and current diet may influence the recall of usual diet (Willett, 1998). In China, cancer patients are commonly advised to avoid or lower meat intake for improving prognosis. Thus, dietary change after cancer diagnosis would probably lead to an underestimation of the association of meat intake with endometrial cancer risk. In our study, the median interval between diagnosis and interview for cases was only 5.6 months. Study participants were asked to report their dietary habits before cancer diagnosis, ignoring any recent dietary changes. This may have minimised the misclassification of the dietary assessment. However, we cannot exclude the possibility that some patients might link meat intake to the cause of their disease and thus the result may have been over-reporting of meat consumption among cases.

In summary, this large population-based case–control study of endometrial cancer, conducted in a population that has a much lower total meat consumption compared to people in Western countries, found that diets high in animal foods increase the risk of endometrial cancer.

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