Published in final edited form as:

Int J Cancer. 2007 April 15; 120(8): 1776–1781.

Nutritional factors in relation to endometrial cancer: A report from a population-based case-control study in Shanghai, China

Wang-Hong Xu^{1,2}, Qi Dai³, Yong-Bing Xiang², Gen-Ming Zhao¹, Zhi-Xian Ruan², Jia-Rong Cheng², Wei Zheng³, and Xiao Ou Shu^{3,*}

1Department of Epidemiology, Fu Dan University School of Public Health, Shanghai, People's Republic of China

2Department of Epidemiology, Shanghai Cancer Institute, Shanghai, People's Republic of China

3Department of Medicine, Vanderbilt Epidemiology Center, Vanderbilt University and Vanderbilt-Ingram Cancer Center, Medical Center East, Nashville, TN

Abstract

We evaluated the role of dietary nutrients in the etiology of endometrial cancer in a population-based case-control study of 1,204 newly diagnosed endometrial cancer cases and 1,212 age frequency-matched controls. Information on usual dietary habits was collected during an in-person interview using a validated, quantitative food frequency questionnaire. Logistic regression analysis was conducted to evaluate the association of nutrients with endometrial cancer risk using an energy density method (e.g., nutrient intake/1,000 kilocalories of intake). Higher energy intake was associated with increased risk, which was attributable to animal source energy and a high proportion of energy from protein and fat. Odds ratios comparing highest versus lowest quintiles of intake were elevated for intake of animal protein (Odds ratio (OR) 5 2.0, 95% confidential interval: 1.5–2.7) and fat (OR 5 1.5, 1.2–2.0), but reduced for plant sources of these nutrients (OR 5 0.7, 0.5–0.9 for protein and OR 5 0.6, 0.5–0.8 for fat). Further analysis showed that saturated and monounsaturated fat intake was associated with elevated risk, while polyunsaturated fat intake was unrelated to risk. Dietary retinol, β -carotene, vitamin C, vitamin E, fiber, and vitamin supplements were inversely associated with risk. No significant association was observed for dietary vitamin B1 or vitamin B2. Our findings suggest that associations of dietary macronutrients with endometrial cancer risk may depend on their sources, with intake of animal origin nutrients being related to higher risk and intake of plant origin nutrients related to lower risk. Dietary fiber, retinol, β -carotene, vitamin C, vitamin E, and vitamin supplementation may decrease the risk of endometrial cancer.

Keywords

endometrial cancer; nutrients; vitamins

High intake of fruits and vegetables has been associated with a reduced risk of endometrial cancer, while high consumption of animal foods has been related to increased risk in a wide variety of populations.^{1–19} However, when the role of nutrients is considered, the evidence is far from consistent.^{5,7,17–19} This may be due to the high correlations that exist between dietary nutrients, which have made it difficult to distinguish the effect of individual nutrients.²⁰ The consensus reached, thus far, is limited to the protective role of low intake of fat and high intake of fiber,^{6,14} both of which may affect women's hormonal milieu.²¹ There is also growing

*Correspondence to: Vanderbilt Epidemiology Center, 6009 Medical Center East, Vanderbilt University, 1215 21st Ave South, Nashville, TN 37232-8300, USA. Fax: +1615-936-1269. E-mail: xiao-ou.shu@vanderbilt.edu

recognition of the potential protective role of β -carotene, vitamin C, and vitamin E in the development of endometrial cancer, though the evidence is not entirely consistent.^{5,9,15}

Most previous reports have come from research conducted in Western populations. Difficulties in assessing nutrient intake from fortified foods, as well as relatively small sample sizes, may have contributed to the controversial literature. More importantly, the dietary sources of nutrient intake were not evaluated^{5,16} or only the source of macronutrients was examined,^{9,12,13,18} making it difficult to disentangle whether it is a dietary pattern or specific nutrients that play a major role in the etiology of endometrial cancer.

In this report, we further evaluated the association of both macro- and micronutrients with endometrial cancer along with their sources (plant or animal origin) in the Shanghai Endometrial Cancer Study (SECS). Unlike their Western counterparts, Chinese women have diets composed mainly of unprocessed and unfortified foods, and they seldom take vitamin supplements. These unique features provided us with an excellent opportunity to evaluate the association of nutrient intake with the development of endometrial cancer.

Material and methods

Subject recruitment

A total of 1,454 newly diagnosed endometrial cancer cases between 30 and 69 years of age, who were permanent residents of urban Shanghai, were identified through the Shanghai Cancer Registry from 1997 through 2003. Cancer diagnosis was confirmed by review of medical charts and available pathologic slides. Of the eligible cases, 1,204 (82.8%) completed an in-person interview. Out of 250 nonparticipants, 135 (9.3%) declined to participate, 66 (4.5%) died before interview, 35 (2.4%) could not be located, or were absent during the study period, and 14 (1.0%) did not participate for other miscellaneous reasons. The median interval between diagnosis and interview for cases was 5.6 months. (interquartile range 5.3–9.2 months).

Potential control subjects were selected randomly from female residents through the Shanghai Resident Registry and frequency-matched to cases by 5-year groups. The age distribution of controls was estimated in advance according to the age distribution of endometrial cancer cases in 1996 (age ranges 30–69). Excluding 59 women who reported previous hysterectomy, 1,629 eligible subjects were identified and 1,212 (74.4%) participated in the study. Reasons for nonparticipation included refusal ($n = 340$, 20.9%), absence during the interview period ($n = 61$, 3.7%), severe illness ($n = 13$, 0.8%), and other miscellaneous reasons ($n = 3$, 0.2%).

Data collection

In-person interviews were completed by trained retired medical professionals. We chose retired medical professionals as interviewers because they can provide medical consultation, draw blood, and are well trusted by the general population. A structured questionnaire was used to collect information on demographic factors, menstrual and reproductive history, hormone use, regular exercise, prior disease history, tobacco and alcohol use, family history of cancer, and height and weight history during adolescence and adulthood. Anthropometrics (weight, height, waist and hip circumferences) were taken during the interview using a standard protocol.²²

Dietary information was gathered using a validated food frequency questionnaire (FFQ),²³ which included 71 common foods and food groups. The questionnaire covered more than 85% of foods commonly consumed in Shanghai. Intake of fruits and vegetables was calculated by weighting the length of time that the food was available on the market during 1 year. Nutrient content from the Chinese Food Composition Tables²⁴ was applied to estimate nutrient intake from all food items and groups. Information on regular use of supplemental vitamins and changes in dietary habits during the week prior to the interview was also obtained.

Calculation of body mass index (BMI) and physical activity in metabolic equivalent tasks (METs), as well as the definition of menopausal status and years of menstruation, have been described in detail in our previous reports.^{22,25}

Data analysis

Nutrients of interest were translated into energy density variables by dividing by calories of intake (nutrient intake/1,000 kilocalories of intake). Nutrients were then classified into quintiles based on their distribution among controls and were treated as dummy variables in regression analyses. Unconditional logistic regression models were applied to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of endometrial cancer risk related to each nutrient. Potential confounders adjusted for in the analysis include age (as a continuous variable), menopausal status (pre/postmenopausal status), BMI (by quintile, as a dummy variable), alcohol consumption (ever/never), physical activity level in METs (by quintile, as dummy variables), diagnosis of diabetes (ever/never), and total energy intake (by quintile, as dummy variables). Additional adjustment for nutrient supplement use (ever/never) did not change the results (data not shown in tables). Additional adjustment for levels of animal food intake (by quintile, as dummy variables) and total fruit and vegetable intake (by quintile, as dummy variables) were conducted during the analysis of dietary vitamin intake stratified by their sources. Trend tests were conducted by assigning an ordinal score (*i.e.*, 1, 2, 3, 4, 5) for the quintile levels of micronutrients and duration of any vitamin use in months (never and quartile duration for users), which was then treated as a continuous variable in the models.

Results

Comparisons of cases and controls on demographic factors and selected traditional risk factors of endometrial cancer are presented in Table I. Compared to controls, women with endometrial cancer were more likely to have a high education level, a family history of cancer, a large body size, a long duration of menstruation, a history of diabetes, a high BMI, and few pregnancies. Cases were less likely than controls to participate in physical activities, to be postmenopausal, to drink alcohol regularly, or to use oral contraceptives. Fewer cases reported having taken vitamin supplements regularly (21.9%) as compared to controls (28.0%).

Table II shows the median intake for selected nutrients and percentage intake of these nutrients from plant food sources among control subjects. Dietary fat, particularly, saturated and monounsaturated fat, and retinol were derived mainly from animal foods (>50%), while plant foods were the major source of other nutrients in this study population. Moderate to high correlations between nutrient intake and animal food intake and nutrient intake and fruit and vegetable intake were observed.

Risk estimates associated with intake of energy and macronutrients are shown in Table III. The ORs (95% CI) for the highest versus lowest intake quintiles were 1.2 (1.0–1.7) for intake of total energy and 1.9 (1.5–2.5) for intake of energy from animal sources. Conversely, a high total energy intake from plant sources was related to a reduced risk with an OR of 0.5 (95% CI: 0.4–0.7). Similar source-dependent association patterns were observed for dietary protein and fat intake. The ORs (95% CI) for the highest versus the lowest quintiles of protein intake were 1.3 (1.0–1.8) for total protein, 2.0 (1.5–2.7) for animal-source protein, and 0.7 (0.5–0.9) for plant-source protein, while the ORs (95% CI) for the highest versus lowest quintiles of fat intake for total, animal-, and plant-sources were 1.1 (0.9–1.5), 1.5 (1.2–2.0), and 0.6 (0.5–0.8), respectively. High intake of saturated fat and monounsaturated fat were related to an increased risk of endometrial cancer, while high intake of dietary fiber was associated with decreased risk. Carbohydrate intake was not associated with endometrial cancer risk. Spline regression analysis indicated that associations of several nutrients with endometrial cancer did not appear to follow a linear dose-response pattern.

Presented in Table IV are ORs of endometrial cancer according to quintile of intake for selected vitamins. After adjusting for potential confounders, cancer risk decreased with increasing intake of retinol, β -carotene, vitamin C, and vitamin E (p for trend <0.05), but was not associated with intake of vitamin B1 (p for trend $=0.37$) or vitamin B2 (p for trend 0.55). Excluding subjects who had ever taken vitamin supplements did not change the results (data not shown).

Further stratified analyses were conducted to see whether the associations of dietary intake of micronutrients were independent of their sources. Significant inverse associations were observed for endometrial cancer risk with animal sources of retinol and plant sources of vitamin E. Neither plant nor animal sources of vitamin B1 or B2 were associated with cancer risk. We did not find a significant association of risk with animal-source vitamin E or plant-source retinol, which may possibly be due to low levels of these micronutrients in these food sources (data not shown).

Table V presents the association between vitamin supplement use and risk of endometrial cancer. A significant 30% reduction in risk of endometrial cancer was observed for subjects who had ever used any vitamin supplement and for those who took multi-vitamins, compared with those who never took any supplements. Furthermore, the risk of cancer decreased with increasing frequency and length of vitamin use (p for trend <0.01). A few study subjects took single vitamin supplements. Compared to those who never used vitamin supplements, supplementation of vitamin C or vitamin E was associated with a nonsignificant 30% reduction in risk, and vitamin B supplementation was associated with a significantly decreased risk of endometrial cancer (OR 5 0.3, 95% CI: 0.1–0.8).

Discussion

In this population-based, case-control study, we found that risk of endometrial cancer increased with increasing intake of total energy, fat, and protein from animal sources, but decreased with increasing intake of these macronutrients from plant sources. Dietary intake of saturated and monounsaturated fat, but not total fat, was associated with an increased risk of endometrial cancer. Intake of dietary fiber, retinol, β -carotene, vitamin C, and vitamin E were associated with decreased risk. No significant associations were observed for intake of carbohydrates, vitamin B1, or vitamin B2.

Energy restriction has been shown to reduce spontaneous and induced tumors, slow tumor growth in rodents,^{26,27} and decrease cellular proliferation by impeding progression of the cell cycle.²⁸ In contrast, a high calorie diet may result in the enhancement of insulin resistance, thus increasing the risk of endometrial cancer.²⁹⁻³¹ Out of 15³⁻¹⁷ published epidemiologic studies, eight,³⁻¹⁰ including one cohort study,¹⁰ have reported that energy intake was positively associated with endometrial cancer risk. A number of investigations,^{6,7,32} including our previous report,⁶ have suggested that only high intake of energy from animal foods was associated with an increased risk of endometrial cancer. In the current study, we found that energy intake from animal foods was positively associated with risk, whereas energy intake from plant foods was negatively related to risk. The positive associations also pertain to dietary protein and fat intake, both of which are found in abundance in animal foods.

It has been suggested that dietary fat increases serum estrogen levels by influencing the metabolism of estrogen and increasing the intestinal re-absorption of estrogen,^{32,33} thus increasing the risk of endometrial cancer, a hormone-dependent disease. Several epidemiologic studies have reported on the adverse effect of dietary fat on disease, independent of obesity.^{17,34} In this report, the association of dietary fat with endometrial cancer depends on its source. That is, fat from animal sources may increase the risk of endometrial cancer, while plant sources

of fat may decrease the risk. These findings do not support Prentice's hypothesis that fat consumption, derived from either animal or plant sources, is directly related to endometrial cancer risk,³⁵ but are consistent with our previous report.⁶ We also observed a positive association for saturated fat and monounsaturated fat. Given that 77.9% of saturated fat and 68.6% of monounsaturated fat, but only 34.2% of polyunsaturated fat, come from animal foods, it would seem that specific types of fat can explain the different effects found for animal and plant sources of fat.

A similar source-dependent association pattern was observed for dietary protein intake in our study. Dietary protein has been implicated in the etiology of endometrial cancer given the high correlation between the incidence of disease and national per capita availability of meat and eggs.^{3,35} Evidence from epidemiologic studies, however, has been limited and controversial.^{6,12,13,16,18,19,32} Earlier studies on protein intake and endometrial cancer risk have found negative^{16,18,19} and positive⁶ associations. One possible mechanism behind the protein-endometrial cancer association is that pyrolytic products generated in the high-temperature cooking of protein-rich foods may be involved in carcinogenesis,³⁶⁻³⁸ and not taking cooking practices into consideration may have contributed to the inconsistent results. It is possible that protein intake may only be a surrogate for pyrolytic substances and the heterocyclic amines (HCAs) produced under high temperature.^{37,38} Another possible explanation for the source-dependent associations of protein, energy, and fat is that source-specific nutrient intake is a surrogate measure for intake of foods rich in these nutrients or minerals.³⁹

Intake of complex carbohydrates was associated with a reduced risk of endometrial cancer in some studies.^{7,13,17} Our study, like others,^{6,14} found that total carbohydrate intake was not associated with endometrial cancer.

The significant inverse association of dietary fiber intake with endometrial cancer observed in our study is in line with previous studies,^{9,12,16} most of which were conducted in Western populations. Dietary fiber intake has been consistently linked to low serum estrogen levels, possibly by decreasing the concentration of intestinal β -glucuronidase, shielding the estrogens excreted in the bile from bacterial deconjugation, inhibiting the intestinal re-absorption of estrogen, and promoting the excretion of estrogen with feces,⁴⁰ thus lowering the risk of endometrial cancer.^{9,12} Female vegetarians, both pre- and postmenopausal, have been shown to have lower urinary excretion of estrogens and lower plasma estrogen levels than omnivores of the same age.^{33,41}

Nutrients such as β -carotene, retinol, vitamin C, and vitamin E may inhibit the development of tumors, including endometrial cancer tumors, by eliciting their antioxidative effects.⁴² However, epidemiologic studies have yielded controversial results.^{5,14-19,43,44} Inverse associations of retinol and β -carotene or vitamin A intake with endometrial cancer have been reported in some studies,^{5,12,18,45} but not in others.^{15,32} The same is true for vitamin C,^{6,13,18,32} and vitamin E.^{5,7} Data regarding the role of vitamins B1 and B2 in the development of endometrial cancer are limited, and no clear association has been documented.^{12,19,46} One possible explanation for these inconsistencies is that it may be partly attributable to the difficulty in disentangling the role of a specific nutrient from that of a dietary pattern. In our study, we adjusted the total amount of animal food intake and total fruit and vegetable intake in the analysis, and further evaluated the association of these nutrients by their sources (plant or animal origin). We found that high intake of retinol, β -carotene, vitamin C, and vitamin E were associated with a decreased risk of endometrial cancer. Inverse associations of vitamin supplement use with cancer risk in our study provide additional evidence on the possible beneficial role of vitamins in the development of the disease.

Several limitations inherent in this study must be addressed. As with all case-control studies, the possibility of recall bias could not be completely eliminated. In our study, however, we tried to minimize recall bias by shortening the interval between diagnosis and interview for cases and by asking the participants to ignore any dietary change over the past year. In addition, because neither study participants nor interviewers were aware of our study hypotheses, recall bias, if any, is likely to be nondifferential, resulting in an underestimation of the nutrient and disease associations. The response rate among controls (74.4%) was lower than that among cases (82.8%), raising the concern of potential selection bias. Unfortunately, this bias cannot be directly assessed in the study due to a lack of information about the nonrespondents. However, our study controls were comparable to the controls of the Shanghai Breast Cancer Study, a study completed in the same population 3 years prior to the current study that had a response rate of 90.3%.⁴⁷ Thus, selection participation bias, although it cannot be ruled out, may not be a major threat to the validity of the study. We implemented several measures to prevent interviewer bias. First, all interviewers received standardized training and were certified to conduct interviews. Second, a standard interview manual was developed and interviewers were instructed to follow the manual strictly. Third, interviewers were not aware of the study hypotheses. Fourth, all interviews were tape-recorded and the contents of each interview were evaluated by a quality control staff member. Similar to all epidemiological studies, measurement errors in dietary assessment are always a concern. Random misclassification of exposure between cases and controls may have biased the associations toward or away from the null. The specific content of multi-vitamin supplements was not available, which may have limited our ability to examine the associations between specific antioxidants and cancer risk. Although careful adjustment was carried out, residual confounding from dietary patterns and other lifestyle factors may still exist.

On the other hand, our study has several strengths. For example, the validated FFQ, the short interval between diagnosis and interview for cases, and the stable dietary pattern in our population have minimized dietary measurement errors. Our study also has benefited from a large sample size, high response rate, low frequency of use of vitamin supplements, and the ability to adjust for a wide range of potential confounders.

In summary, the results of this study suggest that higher intake of energy, protein, and fat from animal sources of food is positively associated with the risk of endometrial cancer. Dietary fiber, retinol, β -carotene, vitamin C, and vitamin E may reduce risk.

Acknowledgements

We thank Dr. Fan Jin for her contributions in implementing the study and Ms. Bethanie Hull and Ms. Brandy Sue Bentley for their assistance in the preparation of this manuscript. We also gratefully acknowledge the dedicated efforts of the study participants and research staff of the Shanghai Endometrial Cancer Study at the Shanghai Cancer Institute.

Grant sponsor: National Cancer Institute (USPHS); Grant number: R01 CA 92585.

References

1. Tao MH, Xu WH, Zheng W, Gao YT, Ruan ZX, Cheng JR, Xiang YB, Shu XO. A case-control study in Shanghai of fruit and vegetable intake and endometrial cancer. *Br J Cancer* 2005;92:2059–64. [PubMed: 15886701]
2. Xu WH, Dai Q, Xiang YB, Zheng W, Zhao GM, Gao YT, Ruan ZX, Cheng JR, Shu XO. Animal food intake and cooking methods in relation to the risk of endometrial cancer in Shanghai women. *Br J Cancer* Dec 4;2006 95(11):1586–92. [PubMed: 17060930]
3. Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *Int J Cancer* 1975;15:617–31. [PubMed: 1140864]
4. Levi F, Franceschi S, Negri E, La Vecchia C. Dietary factors and the risk of endometrial cancer. *Cancer* 1993;71:3575–81. [PubMed: 8490907]

5. Negri E, La Vecchia C, Franceschi S, Levi F, Parazzini F. Intake of selected micronutrients and the risk of endometrial carcinoma. *Cancer* 1996;77:917–23. [PubMed: 8608484]
6. Shu XO, Zheng W, Potischman N, Brinton LA, Hatch MC, Gao YT, Fraumeni JF Jr. A population-based case-control study of dietary factors and endometrial cancer in Shanghai, People's Republic of China. *Am J Epidemiol* 1993;37:155–65. [PubMed: 8452119]
7. Potischman N, Swanson CA, Brinton LA, McAdams M, Barrett RJ, Berman ML, Mortel R, Twigg LB, Wilbanks GD, Hoover RN. Dietary associations in a case-control study of endometrial cancer. *Cancer Causes Control* 1993;4:239–50. [PubMed: 8318640]
8. Kalandidi A, Tzonou A, Lipworth L, Gamatsi I, Filippa D, Trichopoulos D. A case-control study of endometrial cancer in relation to reproductive, somatometric, and life-style variables. *Oncology* 1996;53:354–9. [PubMed: 8784467]
9. Jain MG, Howe GR, Rohan TE. Nutritional factors and endometrial cancer in Ontario, Canada. *Cancer Control* 2000;7:288–96. [PubMed: 10832115]
10. Furberg AS, Thune I. Metabolic abnormalities (hypertension, hyperglycemia and overweight), lifestyle (high energy intake and physical inactivity) and endometrial cancer risk in a Norwegian cohort. *Int J Cancer* 2003;104:669–76. [PubMed: 12640672]
11. Terry P, Baron JA, Weiderpass E, Yuen J, Lichtenstein P, Nyren O. Lifestyle and endometrial cancer risk: a cohort study from the Swedish twin registry. *Int J Cancer* 1999;82:38–42. [PubMed: 10360818]
12. Goodman MT, Hankin JH, Wilkens LR, Lyu LC, McDuffie K, Liu LQ, Kolonel LN. Diet, body size, physical activity, and the risk of endometrial cancer. *Cancer Res* 1997;57:5077–85. [PubMed: 9371506]
13. Zheng W, Kushi LH, Potter JD, Sellers TA, Doyle TJ, Bostick RM, Folsom AR. Dietary intake of energy and animal foods and endometrial cancer incidence. The Iowa women's health study. *Am J Epidemiol* 1995;142:388–94. [PubMed: 7625403]
14. Tzonou A, Lipworth L, Kalandidi A, Trichopoulou A, Gamatsi I, Hsieh CC, Notara V, Trichopoulos D. Dietary factors and the risk of endometrial cancer: a case-control study in Greece. *Br J Cancer* 1996;73:1284–90. [PubMed: 8630294]
15. Jain MG, Rohan TE, Howe GR, Miller AB. A cohort study of nutritional factors and endometrial cancer. *Eur J Epidemiol* 2000;16:899–905. [PubMed: 11338120]
16. McCann SE, Freudenheim JL, Marshall JR, Brasure JR. Diet in the epidemiology of endometrial cancer in Western New York (United States). *Cancer Causes Control* 2000;11:965–74. [PubMed: 11142531]
17. Littman AJ, Beresford SA, White E. The association of dietary fat and plant foods with endometrial cancer (United States). *Cancer Causes Control* 2001;12:691–702. [PubMed: 11562109]
18. Barbone F, Austin H, Partridge EE. Diet and endometrial cancer: a case-control study. *Am J Epidemiol* 1993;137:393–403. [PubMed: 8460621]
19. Salazar-Martinez E, Lazcano-Ponce E, Sanchez-Zamorino LM, Gonzalez-Lira G, Escudero-De Los Rios P, Hernandez-Avila M. Dietary factors and endometrial cancer risk. Results of a case-control study in Mexico. *Int J Gynecol Cancer* 2005;15:938–45. [PubMed: 16174249]
20. Block G. Human dietary assessment: methods and issues. *Prev Med* 1989;18:653–60. [PubMed: 2616545]
21. Purdie DM, Green AC. Epidemiology of endometrial cancer. *Best Pract Res Clin Obstet Gynaecol* 2001;15:341–54. [PubMed: 11476557]
22. Xu WH, Matthews CE, Xiang YB, Zheng W, Ruan ZX, Cheng JR, Gao YT, Shu XO. Effect of adiposity and fat distribution on endometrial cancer risk in Shanghai women. *Am J Epidemiol* 2005;16:939–47. [PubMed: 15870158]
23. Shu XO, Yang G, Jin F, Kushi L, Liu D, Wen W, Gao YT, Zheng W. Validity and reproducibility of food frequency questionnaire used in the Shanghai women's health study. *Eur J Clin Nutr* 2004;58:17–23. [PubMed: 14679362]
24. Yang, YX.; Wang, GY.; Pang, XC., editors. China food composition 2002. Beijing University Medical Press; Beijing: 2002.
25. Matthews CE, Xu WH, Zheng W, Gao YT, Ruan ZX, Cheng JR, Xiang YB, Shu XO. Physical activity and risk of endometrial cancer: a report from the Shanghai endometrial cancer study. *Cancer Epidemiol Biomarkers Prev* 2005;14:779–85. [PubMed: 15824143]

26. Weindruch R. Dietary restriction, tumors, and aging in rodents. *J Gerontol* 1989;44:67–71. [PubMed: 2681366]
27. Rogers AE. Diet and breast cancer: studies in laboratory animals. *J Nutr* 1997;127(Suppl 5):933S–935S. [PubMed: 9164267]
28. Thompson HJ, Jiang W, Zhu Z. Mechanisms by which energy restriction inhibits carcinogenesis. *Adv Exp Med Biol* 1999;470:77–84. [PubMed: 10709676]
29. Stoll BA. New metabolic-endocrine risk markers in endometrial cancer. *Br J Obstet Gynaecol* 1999;106:402–6. [PubMed: 10430187]
30. Lee PD, Giudice LC, Conover CA, Powell DR. Insulin-like growth factor binding protein-1: recent findings and new directions. *Proc Soc Exp Biol Med* 1997;216:319–57. [PubMed: 9402139]
31. Troisi R, Potischman N, Hoover RN, Siiteri P, Brinton LA. Insulin and endometrial cancer. *Am J Epidemiol* 1997;146:476–82. [PubMed: 9290508]
32. Lissner L, Kroon UB, Bjorntorp S, Bloks S, Wilhelmsen L, Silverstolpe G. Adipose tissue fatty acids and dietary fat sources in relation to endometrial cancer: a retrospective study of cases in remission, and population-based controls. *Acta Obstet Gynecol Scand* 1993;72:481–7. [PubMed: 8394629]
33. Gorbach SL, Goldin BR. Diet and the excretion and enterohepatic cycling of estrogens. *Prev Med* 1987;16:525–31. [PubMed: 3628202]
34. La Vecchia C, Decarli A, Fasoli M, Gentile A. Nutrition and diet in the etiology of endometrial cancer. *Cancer* 1986;57:1248–53. [PubMed: 3002600]
35. Prentice RL, Sheppard L. Dietary fat and cancer: consistency of the epidemiologic data, and disease prevention that may follow from a practical reduction in fat consumption. *Cancer Causes Control* 1990;1:81–97. [PubMed: 2102280]discussion 99–109
36. Visek WJ, Clinton SK, Imrey PB, Thursh DR, Truex CR, Alster JM, Anderson PA, Mabry FJ, Nandkumar S, Simon J. Dietary protein and chronic toxicity of 1,2-dimethylhydrazine fed to mice. *J Toxicol Environ Health* 1991;32:383–413. [PubMed: 2016752]
37. de Meester C, Gerber GB. The role of cooked food mutagens as possible etiological agents in human cancer. A critical appraisal of recent epidemiological investigations. *Rev Epidemiol Sante Publique* 1995;43:147–61. [PubMed: 7732201]
38. Weisburger, JH.; Barnes, WS.; Czerniak, R. Mutagens and carcinogens in food. In: Reddy, BS.; Cohen, LA., editors. *Diet, nutrition and cancer: a critical evaluation*, vol 2: Micronutrient, nonnutritive dietary factors, and cancer. CRC Press; Boca Raton, FL: 1989. p. 115–34.
39. Willett WC. Total energy intake and nutrient composition: dietary recommendations for epidemiologists. *Int J Cancer* 1990;46:770–1. [PubMed: 2228304]
40. Rose DP. Dietary fiber and breast cancer. *Nutr Cancer* 1990;13:1–8. [PubMed: 2153951]
41. Goldin BR, Adlercreutz H, Gorbach SL, Warram JH, Dwyer JT, Swenson L, Woods MN. Estrogen excretion patterns and plasma levels in vegetarian and omnivorous women. *N Engl J Med* 1982;307:1542–7. [PubMed: 7144835]
42. Steinmetz KA, Potter JD. Vegetables, fruit, and cancer prevention: a review. *J Am Diet Assoc* 1996;96:1027–39. [PubMed: 8841165]
43. World Cancer Research Fund in association with the American Institute for Cancer Research. *World Cancer Research Fund*; Washington, DC: 1997. Food, nutrition and the prevention of cancer: a global perspective.
44. Hill HA, Astin H. Nutrition and endometrial cancer. *Cancer Causes Control* 1996;7:19–32. [PubMed: 8850432]
45. Petridou E, Kedikoglou S, Koukoulomatis P, Dessypris N, Trichopoulos D. Diet in relation to endometrial cancer risk: a case-control study in Greece. *Nutr Cancer* 2002;44:16–22. [PubMed: 12672637]
46. Terry P, Vainio H, Wolk A, Weiderpass E. Dietary factors in relation to endometrial cancer: a nationwide case-control study in Sweden. *Nutr Cancer* 2002;42:25–32. [PubMed: 12235647]
47. Dai Q, Shu XO, Jin F, Potter JD, Kushi LH, Teas J, Gao YT, Zheng W. Population-based case-control study of soyfood intake and breast cancer risk in Shanghai. *Br J Cancer* 2001;85:372–8. [PubMed: 11487268]

TABLE I
COMPARISON OF CASES AND CONTROLS ON DEMOGRAPHIC CHARACTERISTICS AND
SELECTED RISK FACTORS, SHANGHAI ENDOMETRIAL CANCER STUDY, 1997–2003

	Cases (<i>n</i> = 1,204)	Controls (<i>n</i> = 1,212)	<i>p</i> value
Age (Means ± SD)	54.5 ± 8.5	54.6 ± 8.5	0.77
Education level (%)			
No formal education	7.9	11.0	
Elementary	14.1	13.0	
Junior high school	37.0	36.4	
High school	25.8	26.9	
Post-high school/college	15.1	12.8	0.05
Physical activity in METs (means ± SD)	10.5 ± 7.3	11.0 ± 4.6	0.05
Oral contraceptive use (%)	18.5	24.9	<0.01
Cancer history among first-degree relatives (%)	35.2	27.9	<0.01
Nulliparity (%)	7.4	3.6	<0.01
Number of pregnancies (means ± SD)	2.6 ± 1.5	2.9 ± 1.5	<0.01
BMI (kg/m ²) (means ± SD)	25.7 ± 4.2	23.8 ± 3.5	<0.01
Alcohol consumption (%)	2.8	5.4	<0.01
Diabetes	15.3	6.9	<0.01
Years of menstruation (means ± SD)	32.8 ± 4.9	30.6 ± 5.4	<0.01
Menopause (%)	58.3	63.1	0.01
Hormone replacement therapy (%)	4.4	4.0	0.66
Fruit and vegetable intake (means ± SD)	553.6 ± 315.9	548.5 ± 326.8	0.70
Animal food intake (g/d) (means ± SD)	195.3 ± 107.5	172.8 ± 100.8	<0.01
Any vitamin supplement use (%)	21.9	28.0	<0.01

Missing values have been excluded. *p* value for *t* test (continuous variables) or χ^2 test (categorical variables).

TABLE II
DIETARY INTAKE OF SELECTED NUTRIENTS AMONG CONTROLS, SHANGHAI ENDOMETRIAL
CANCER STUDY, 1997–2003

Nutrient intake per day	Median (25th, 75th percentile)	Percentage from plant foods	Partial correlation coefficients adjusted for energy intake with intake of	
			Fruits and vegetables	Animal foods
Energy intake (kcal)	1708 (1426, 2016)	82.1	0.41 ^I	0.62 ^I
Macronutrients (g)				
Protein	67.7 (54.4, 83.4)	63.7	0.29	0.75
Fat	30.7 (22.3, 40.6)	40.7	0.02	0.63
Saturated fat	8.9 (6.2, 11.9)	25.1	−0.03	0.68
Monounsaturated fat	12.5 (8.9, 17.6)	25.5	−0.04	0.64
Polyunsaturated fat	7.9 (5.6, 10.7)	67.4	0.15	0.36
Carbohydrate	283.8 (241.5, 332.7)	97.5	−0.11	−0.76
Dietary fiber	10.8 (8.2, 13.9)	100.0	0.76	0.01
Micronutrients				
β-Carotene (μg)	2639.3 (1726.7, 3783.1)	100.0	0.80	0.09
Retinol (μg)	153.6 (89.2, 223.2)	3.4	0.06	0.46
Vitamin B1 (mg)	0.89 (0.73, 1.08)	71.9	0.43	0.26
Vitamin B2 (mg)	0.87 (0.66, 1.09)	59.0	0.53	0.56
Vitamin C (mg)	80.2 (54.8, 115.2)	100.0	0.91	0.12
Vitamin E (mg)	13.9 (10.0, 18.5)	85.1	0.41	0.12

^I Not adjusted for energy intake.

ODDS RATIOS FOR ENDOMETRIAL CANCER ACCORDING TO QUINTILE OF ENERGY AND MACRONUTRIENT INTAKE, SHANGHAI
ENDOMETRIAL CANCER STUDY, 1997–2003

Nutrients	Dietary macronutrient intake (by quintile)				
	Q1 (low)	Q2	Q3	Q4	Q5 (high)
<i>Energy intake</i>					
Total energy intake (kcal/d)	1.0	1.0 (0.8–1.4)	1.1 (0.8–1.4)	1.1 (0.8–1.4)	1.2 (1.0–1.7)
Percentage from animal food	1.0	1.5 (1.1–1.9)	1.7 (1.3–2.3)	1.6 (1.2–2.1)	1.9 (1.5–2.5)
Percentage from plant food	1.0	0.8 (0.6–1.1)	0.9 (0.7–1.2)	0.8 (0.6–1.0)	0.5 (0.4–0.7)
<i>Macronutrient intake (g/1,000 kcal/d)</i>					
Total protein intake	1.0	1.0 (0.7–1.3)	1.0 (0.7–1.3)	1.2 (0.9–1.6)	1.3 (1.0–1.8)
Animal protein	1.0	1.4 (1.0–1.8)	1.6 (1.2–2.1)	2.0 (1.5–2.7)	2.0 (1.5–2.7)
Plant protein	1.0	1.1 (0.9–1.4)	1.1 (0.8–1.4)	0.8 (0.6–1.0)	0.7 (0.5–0.9)
Total fat intake	1.0	1.2 (0.9–1.5)	1.1 (0.8–1.5)	1.3 (1.0–1.7)	1.1 (0.9–1.5)
Animal fat	1.0	1.2 (0.9–1.6)	1.7 (1.3–2.2)	1.6 (1.2–2.0)	1.5 (1.2–2.0)
Plant fat	1.0	1.1 (0.8–1.4)	1.1 (0.9–1.5)	0.8 (0.6–1.0)	0.6 (0.5–0.8)
Saturated fat	1.0	1.2 (0.9–1.6)	1.4 (1.0–1.8)	1.3 (1.0–1.8)	1.3 (1.0–1.7)
Monounsaturated fat	1.0	1.3 (1.0–1.8)	1.6 (1.2–2.1)	2.0 (1.5–2.6)	1.4 (1.1–1.9)
Polyunsaturated fat	1.0	1.2 (0.9–1.5)	1.0 (0.8–1.3)	1.1 (0.8–1.4)	0.8 (0.6–1.1)
Carbohydrates	1.0	1.0 (0.8–1.3)	0.9 (0.7–1.2)	1.0 (0.8–1.3)	0.8 (0.6–1.0)
Dietary fiber	1.0	0.9 (0.7–1.1)	0.9 (0.7–1.1)	0.7 (0.5–0.9)	0.8 (0.6–1.0)

Quintile cut points were 1,382, 1,603, 1,816, 2,077 kcal/d for total energy intake; 10.7, 15.4, 19.4, 24.3 for percentage from animal food; 75.7, 80.6, 84.6, 89.3 for percentage from plant food; 34.8, 38.0, 41.2, 45.3 g/1,000 kcal/d for total protein intake; 9.2, 12.8, 15.9, 20.6 g/1,000 kcal/d for animal protein intake; 21.6, 23.7, 25.7, 28.1 g/1,000 kcal/d for plant protein intake; 13.8, 16.9, 19.5, 23.1 g/1,000 kcal/d for total fat intake; 6.8, 9.5, 12.2, 15.6 g/1,000 kcal/d for animal fat intake; 5.0, 6.2, 7.4, 9.0 g/1,000 kcal/d for plant fat intake; 3.6, 4.8, 5.8, 7.0 g/1,000 kcal/d for saturated fat intake; 5.3, 6.7, 8.2, 10.3 g/1,000 kcal/d for monounsaturated fat intake; 3.4, 4.3, 5.0, 6.1 g/1,000 kcal/d for polyunsaturated fat intake; 152.7, 164.3, 172.8, 183.7 g/1,000 kcal/d for carbohydrate intake and 4.8, 5.8, 6.9, 8.1 g/1,000 kcal/d for dietary fiber intake. Adjusted for age, education, menopausal status, diagnosis of diabetes, alcohol consumption, physical activity, body mass index, and total energy intake.

ODDS RATIOS FOR ENDOMETRIAL CANCER ACCORDING TO QUINTILE OF SELECTED VITAMINS, SHANGHAI ENDOMETRIAL CANCER STUDY, 1997–2003

	Nutrient intake (by quintile, amount per 1,000 kcal per day)					<i>p</i> for trend
	Q1 (low)	Q2	Q3	Q4	Q5 (high)	
Retinol (μg)	1.0	0.7 (0.5–0.9)	0.7 (0.5–1.0)	0.7 (0.5–0.9)	0.6 (0.4–0.8)	0.02
β-Carotene (μg)	1.0	1.0 (0.7–1.3)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.6 (0.4–0.8)	<0.01
Vitamin B1 (mg)	1.0	0.8 (0.6–1.1)	0.7 (0.6–1.0)	0.8 (0.6–1.0)	0.9 (0.6–1.2)	0.37
Vitamin B2 (mg)	1.0	0.9 (0.7–1.3)	0.8 (0.6–1.1)	0.7 (0.5–1.0)	1.0 (0.7–1.4)	0.55
Vitamin C (mg)	1.0	0.9 (0.6–1.2)	0.6 (0.4–0.9)	0.6 (0.4–0.9)	0.5 (0.3–0.7)	<0.01
Vitamin E (mg)	1.0	1.1 (0.8–1.4)	1.0 (0.7–1.3)	0.8 (0.6–1.1)	0.8 (0.6–1.1)	0.03

Adjusted for age, education, menopausal status, diagnosis of diabetes, alcohol consumption, BMI, physical activity, total animal food intake, total fruit and vegetable intake, and total energy intake. Quintile cut points were 50.3, 74.6, 100.6, 137.3 μg/1,000 kcal/d for retinol intake; 922, 1,359, 1,793, 2439 μg/1,000 kcal/d for β-carotene intake; 0.46, 0.50, 0.54, 0.59 mg/1,000 kcal/d for vitamin B1 intake; 0.39, 0.47, 0.54, 0.62 mg/1,000 kcal/d for vitamin B2 intake; 29.8, 41.6, 54.4, 72.7 mg/1,000 kcal/d for vitamin C intake, and 6.0, 7.4, 8.8, 10.4 mg/1,000 kcal/d for vitamin E intake.

TABLE V
ASSOCIATIONS OF VITAMIN SUPPLEMENT USE WITH THE RISK OF ENDOMETRIAL CANCER,
SHANGHAI ENDOMETRIAL CANCER STUDY, 1997–2003

	Cases/controls	OR (95% CI)	<i>p</i> for trend
<i>Vitamin supplement use</i>			
Never	940/873	1.0 (ref.)	
Ever	264/339	0.7 (0.6–0.9)	
Multi vitamin use	179/226	0.7 (0.6–0.9)	
Only vitamin C	20/23	0.7 (0.4–1.3)	
Only vitamin A	1/0	–	
Only vitamin E	56/71	0.8 (0.5–1.1)	
Only B vitamins	8/19	0.3 (0.1–0.8)	
<i>Duration of any vitamin use (months)</i>			
Never	940/873	1.0 (ref.)	
≤336	86/97	0.8 (0.6–1.2)	
337–840	52/74	0.6 (0.4–0.9)	
841–1,680	76/103	0.7 (0.5–0.9)	
>1,680	50/65	0.6 (0.4–0.9)	<0.01

Adjusted for age, education, menopausal status, diagnosis of diabetes, alcohol consumption, physical activity, and BMI.