Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

HHS Public Access

Author manuscript

Nutr Cancer. Author manuscript; available in PMC 2017 May 22.

Published in final edited form as:

Nutr Cancer. 2015 ; 67(1): 89–97. doi:10.1080/01635581.2015.976319.

Association of dietary glycemic index and glycemic load with endometrial cancer risk among Chinese women

Wang Hong Xu[1], **Yong-Bing Xiang**[2], **Xianglan Zhang**[3], **Zhixian Ruan**[2], **Hui Cai**[3], **Wei Zheng**[3], and **Xiao-Ou Shu**[3]

[1]Department of Epidemiology, School of Public Health, Fudan University, Shanghai, 200032, People's Republic of China

[2]Department of Epidemiology, Shanghai Cancer Institute, Renji Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, 200032, People's Republic of China

[3]Vanderbilt Epidemiology Center, Department of Medicine and Vanderbilt-Ingram Cancer Center, 8th floor, 2525 West End Ave, Nashville, TN 37232-8300, United States

Abstract

We evaluated the association of dietary glycemic-index (GI) and glycemic-load (GL) with the risk of endometrial cancer in a population-based, case-control study of 1,199 endometrial cancer patients and 1,212 age-frequency-matched controls in urban Shanghai, China, where diets are typically high in carbohydrates and have a high GL. Information on dietary habits, physical activity, and other relevant information was collected using a validated questionnaire, and anthropometric measurements were taken. Logistic regression was applied in the analysis. Dietary GI was independently associated with risk for endometrial cancer but GL and carbohydrate intake was unrelated to the risk. Multivariable-adjusted odds ratios (ORs) for increasing quartiles of intake were 1.0, 1.2, 1.4, and 1.4 (95% CI: 1.0–2.0) for dietary GI (P_{trend}: 0.07). High intake of staples, especially rice, was positively associated with endometrial cancer. The association with GI was more evident among lean and normal weight women, although the test for interaction was not significant. This study suggests that intake of high GI foods, but not carbohydrates per se, may increase risk for endometrial cancer.

Keywords

carbohydrates; diet; endometrial cancer; glycemic index; glycemic load

Correspondence should be addressed to: Dr. Xiao Ou Shu, M.D., Ph.D. Vanderbilt Epidemiology Center, Institute of Medicine & Public Health, Vanderbilt University Medical Center, 2525 West End Avenue, Suite 600 (IMPH), Nashville, TN 37203-1738, Tel: 615-936-0713, Fax: 615-936-8291, Xiao-ou.shu@vanderbilt.edu.

Author Contributions: WHX wrote the manuscript, performed the statistical analyses, and supervised data and sample collection; YBX contributed to the study design and field operations; XZ contributed to the data analysis and result interpretation, ZR contributed to the field operations; HC contributed to the data analysis; WZ and XOS conceived of and designed the study and contributed to manuscript revision. XOS had primary responsibility for the final content.

Conflict of interest: The authors have no conflicts of interest to declare.

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

INTRODUCTION

Non-genetic, lifestyle factors may account for more than 75% of endometrial cancer cases and represent potential targets for prevention of this disease [1]. Dietary factors, particularly high intake of foods with a high glycemic index (GI), are logical choices for prevention, because they have been clearly linked to insulin resistance and hyperinsulinemia [2]. Insulin resistance induced by diet may play a particularly pernicious role in the development of endometrial cancer, possibly by reducing levels of sex-hormone binding globulin and insulin-like growth factor binding proteins (IGFBP), which ultimately increases the bioavailability of sex-hormones and IGF-1 [3].

Epidemiological evidence linking high GI and glycemic load (GL) diets with the risk of endometrial cancer has been previously reported [4–10], and there are suggestions that the associations may differ according to menopausal status, body size, or physical activity [4–7,11]. However, all previous studies have been conducted in Europe and North America [8–12], where bread, potatoes, sugar-sweetened soft drinks, sweets, and desserts are the main sources of dietary GL. Asian women traditionally consume diets high in carbohydrates and have rice as the major staple food [13], but the effect of these factors on this disease has not been evaluated in this population.

In this report, which is among the largest endometrial cancer studies with comprehensive assessment of dietary exposures, we evaluate the role of total carbohydrate intake, overall GI, and total GL in the development of endometrial cancer and their potential interactions with menopausal status, body size, and physical activity among Chinese women.

MATERIALS AND METHODS

Study design

The Shanghai Endometrial Cancer Study is a population-based, case-control study conducted among 30–69 year-old residents of Shanghai, China, recruited between 1997 and 2003. Through the Shanghai Cancer Registry, 1,449 eligible cases were identified and 1,199 (82.7%) participated in the study. The diagnosis of each case was confirmed by medical chart review and review of available pathology slides by senior study pathologists. Among the 250 cases who did not participate, 135 refused (9.3%), 66 died before interview (4.5%), 23 (1.6%) could not be located, 12 were out of town during the time interviews were conducted (0.8%), and 14 could not be interviewed for other miscellaneous reasons (1.0%). The median interval between diagnosis and interview for cases was 5.6 months (inter-quartile range=3.4 to 9.2 months).

Controls were randomly selected from the Shanghai Resident Registry and were frequency-matched to cases on age based on the age distribution of endometrial cancer cases from registration data available when the study was initiated (1996). After exclusion of 59 women who had reported a hysterectomy, 1,212 of 1,629 eligible controls were included in the study (74.4%). Reasons for non-participation among controls were refusal (n=340, 20.9%), being out of town during the time interviews were conducted (n=61, 3.7%), severe illness (n=13, 0.8%), and other miscellaneous reasons (n=3, 0.2%). Approval was obtained from the

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

institutional review boards of all participating institutions prior to the initiation of the study, and written, informed consent was obtained from all study participants prior to interview.

Retired nurses and physicians were trained to conduct in-person interviews and complete all measurements for the study. A structured questionnaire was employed to assess demographic characteristics, menstrual and reproductive events, exogenous hormone use, dietary habits, personal lifestyle, family cancer history, physical activity, occupational history, and weight history. Menopause was defined as the cessation of the menstrual period for at least 12 months before diagnosis for cases and interview for controls, excluding lapses caused by pregnancy, breastfeeding, or estrogen use.

Dietary assessment

Dietary intake was assessed using a food frequency questionnaire (FFQ) that was specifically developed for evaluation of dietary intake in this study population [13]. The time-frame of the assessment was the 5-year period before the reference date (diagnosis date for cases and interview date for controls). The FFQ asked participants how frequently they ate a specific food or food group (i.e., per day, week, month, year, or never), followed by a question to capture the amount of food they ate in *liang* (1 *liang*=50 grams). For vegetable intake, participants were asked to describe their consumption during the month(s) when the vegetable was available, and average daily intakes of these foods were estimated by weighting the percentage of months that the study participants consumed the particular vegetable over a one-year period. Using these FFQ data, the amount of food consumed (grams/day) was estimated. Daily intake of total energy, carbohydrates, and other nutrients were then calculated based on the Chinese Food Composition Tables and the amount of food consumed [14]. Our validation study indicated that nutrient and food intake derived from the FFQ and multiple 24-hr dietary recalls correlated reasonably well, with correlation coefficients of 0.64 and 0.66 for intake of total energy and carbohydrates, respectively [13].

As described in detail previously [15,16], dietary GI and GL for each participant was calculated based on the validated FFQ [13]. The GI value for each food was obtained from the Chinese Food Composition Tables [14] and supplemented by international tables for GI values [17]. Each food's GL was calculated by multiplying the food's GI value by the carbohydrate content of the food and the average amount of the food consumed per day. Total dietary GL was then produced by summing these products over all food items. Dietary GI was derived by dividing the dietary GL by the amount of carbohydrate intake, thus yielding a weighted average GI for each individual's diet [15].

Physical activity assessment

Quantitative estimates of non-occupational physical activity have been described elsewhere [18]. Briefly, energy expenditure was calculated for each reported activity in metabolic equivalent task-hours (MET-hrs) [19], and summary energy expenditure values (MET-hrs/d) for each reported activity were calculated as an average over the time interval assessed. The validation study of a similar physical activity questionnaire has indicated reasonable validity for our indices in Chinese women [20].

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Body size assessment

Body mass index (BMI: weight in kilograms divided by height in meters squared, kg/m^2) and waist-to-hip circumference ratio (WHR) were calculated from direct measurements at the time of the interview using a standardized protocol [21]. Waist circumference was measured at a level of 2.5 cm above the umbilicus, and hip circumference was defined as the maximum girth reading between waist and thigh.

Statistical analyses

Statistical analyses were conducted utilizing SAS statistical software 9.1 (SAS Institute Inc., Cary, NC). Distributions of demographic and suggested risk factors between cases and controls were evaluated using Chi-square or *t* tests. An unconditional logistical regression model was applied to evaluate the associations of GI and GL with the risk of endometrial cancer with adjustment for potential confounders, which included age (yrs), per-capita income (< 4166.67, 4166.68–6250.00, 6250.01–8750.00 and > 8750.00 RMB *yuan*), menopausal status (pre-/post-menopausal), diagnosis of diabetes (ever/never), BMI (in quartiles), non-occupational physical activity (MET-hrs/d, in quartiles), energy intake (kcal/d, continuous variable), intake of dietary fiber (g/d, in quartiles), protein (g/d, in quartiles) and fat (g/d, in quartiles). Mutual adjustment of GI and GL was further conducted so that their independent effects could be evaluated. Tests for linear trend were performed by entering the categorical variables as continuous parameters in the adjusted models. Tests for multiplicative interaction were performed by including two main effects and a cross-product term in the regression model. All statistical tests were based on two-sided probability.

RESULTS

As described in our previous studies [18,21], cases and controls were similar with respect to age, tobacco smoking status, and use of hormone replacement therapy. Compared with controls, cases were more likely to have attained more education, to have an earlier age at menarche, later age at menopause, and thus more total years of menstruation. Cases were also more likely to have been diagnosed with diabetes, to have a family history of cancer, fewer pregnancies, and a higher BMI and WHR, but were less likely to have ever consumed alcohol, used oral contraceptives, or engaged in regular physical activity.

GL was highly correlated with total carbohydrate intake. Among controls, the Pearson correlation coefficient between carbohydrate intake and GL was 0.96 (P<0.0001). GI was significantly correlated with GL (correlation coefficient: 0.32, P<0.0001) and carbohydrate intake (correlation coefficient: 0.05, P=0.02). As presented in Table 1, dietary GL was positively associated with intake of carbohydrates, fats, protein, and fiber. Women in the higher quartiles of GL were more likely to have a lower annual income and be postmenopausal, but they were less likely to have a history of diabetes. They also had more non-occupational physical activity. GL was also positively associated with overall obesity (Table 1).

In this study, we evaluated the association of total carbohydrate intake with the risk of endometrial cancer using a standard multivariate model, nutrient residual model, and

Author Manuscript

multivariate nutrient density model [22]. In the nutrient residual model, the residual method described by Willett and Stampfer [23] was applied to reduce measurement error and to adjust for extraneous variation owing to total energy intake. As shown in Table 2, none of the three approaches yielded a significant association between energy intake adjusted for total carbohydrate consumption and endometrial cancer risk before or after adjustment for other covariates.

On the other hand, excess risk for endometrial cancer was observed for high dietary GI and high GL intake (Table 3). The age-adjusted ORs (95%CI) for the highest versus lowest intake quartiles were 1.4 (95%CI: 1.1–1.7) for GL and 1.3 (95%CI: 1.0–1.6) for GI. Multivariable adjustment attenuated the positive association of GL with cancer risk, with multivariable adjusted ORs across increasing quartiles of intake being 1.0, 1.1, 1.1, and 1.3 (95% CI: 0.9–1.9) for dietary GL (*P* for trend=0.21) and 1.0, 1.2, 1.4 and 1.4 (95%CI: 1.0–1.9) for dietary GI (*P* for trend=0.03). After further mutually adjusting for GL and GI, ORs for increasing quartiles of intake were 1.0, 1.0, 1.0, and 1.1 (95% CI: 0.7–1.7) for GL (*P* for trend= 0.83), and 1.0, 1.2, 1.4, and 1.4 (95% CI: 1.0–2.0) for GI (*P* for trend= 0.07), as shown in Table 3.

The top 10 contributors to dietary GL in this population were rice (79.1%), noodles and steamed bread (7.7%), sweets and desserts (3.3%), bread (2.2%), watermelon (1.6%), potatoes (0.7%), candy (0.6%), apples (0.6%), sweet potatoes (0.4%), and milk (0.4%). We further evaluated the associations of high GI foods with endometrial cancer risk and found that high intake of staples (rice, noodles and steamed bread, and bread) was associated with an increase in endometrial cancer risk. Compared with women in the lowest quartile of intake, the adjusted ORs for endometrial cancer risk across quartiles were 1.0, 1.4, 1.3, and 1.5 (95% CI, 1.1–2.2) for staples (*P* for trend=0.03). The positive association was more pronounced for rice consumption, the most important contributor to dietary GL in this population. The OR comparing extreme categories of rice intake (<200 g/d vs. ≥300 g/d) was 1.7 (95% CI, 1.2–2.5). Intake of tubers (potatoes and sweet potatoes) was not associated with risk for endometrial cancer in this study.

Postmenopausal status, higher BMI, and physical inactivity are known risk factors for endometrial cancer and were associated with increased risk for endometrial cancer in our population [18,21]. These factors are also major determinants of sex-hormone levels and are related to insulin resistance [3]. Therefore, we conducted further analyses stratified by these factors. Neither menopausal status nor physical activity modified the dietary associations under study (data not shown). Given that a BMI cut point of 23 instead of 25 has been recommended for use among Asian women to define overweight status [24], we applied both in the stratified analysis (Table 4). We found that the positive association of GL, GI and rice intake with cancer appeared to be more pronounced among women with lower BMI. However, the test for multiplicative interaction between BMI and GI was significant only when a BMI cut-point of 23 was applied (*P* for interaction=0.03) (Table 4).

We carried out further analyses to evaluate whether age at diagnosis (using cut-points of 45, 50, 55 and 60 years old) modified the observed associations of GI and GL with endometrial

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

cancer risk. We did not find any evidence of interaction in either pre- or post- menopausal women (data not shown in the tables).

DISCUSSION

Endometrial cancer is a hormone-dependent disease and has been consistently associated with obesity. Evidence is accumulating that insulin resistance and hyperinsulinemia play an important role in the etiology of endometrial cancer [3]. Recently, it has been suggested that a moderately high-carbohydrate, low-GI diet may prevent insulin resistance and polycystic ovarian syndrome in women [25]. This suggests a potential role for the glycemic nature of a diet in the incidence of endometrial cancer.

Dietary GI and GL are two physiological indexes of the metabolic effects of dietary carbohydrates [17,26]. While GI is used to characterize foods that contain carbohydrates according to their postprandial blood glucose response, and hence their effect on blood insulin levels [26–28], GL was introduced to quantify the overall estimate of postprandial glycemia by combining the GI value and the quantity of carbohydrates consumed [17,28]. Consumption of foods with a high GI may increase insulin secretion rapidly, which may, in turn, induce insulin resistance and predispose individuals to type 2 diabetes, cancers, including endometrial cancer, and other diseases [26–28,12,29].

Epidemiological evidence for a direct association between high GI foods and endometrial cancer risk is limited but rather consistent. While almost all studies observed a null association between total carbohydrate intake and endometrial cancer [29,5–7], four of eight related studies, including one case-control [4] and three cohort studies [6,7,10], reported a positive association of GL with the risk of endometrial cancer. Of the two cohort studies that observed an overall null association [5,29], the European Prospective Investigation into Cancer and Nutrition Cohort (EPIC) study observed a modifying effect of hormone replacement therapy use on associations of GL with endometrial cancer risk, such that GL was associated with higher risk for never users [29]. The Swedish Mammography Cohort study found a 3-fold increased risk of endometrial cancer for the highest versus lowest extreme quartiles of GL intake among overweight women (BMI $\geq$ 25 kg/m^2) with low physical activity levels [5]. The positive GL-cancer association was reported to be more pronounced among premenopausal women [6], obese women [6], and non-diabetic women [7]. On the other hand, a positive association of GI with endometrial cancer was observed only in case-control studies [4,8,9] and the association was much weaker [6] or absent [5,7,10,29] in cohort studies.

We found that the positive associations of GI and GL intake with endometrial cancer risk were statistically significant before adjusting for known risk factors for endometrial cancer. This result is consistent with most previous studies [4,6,7]. However, multivariate adjustment attenuated the positive association of cancer risk with GL but strengthened the association with GI. Further mutual adjustment of GI and GL did not change the association of cancer risk with GI, but eliminated the association with GL. This result, as well as the null association of carbohydrate intake with endometrial cancer risk, suggests that in this

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

population, the quality of the carbohydrates consumed may play a more important role in the development of endometrial cancer than the quantity of carbohydrates consumed.

In our study, age at diagnosis, menopausal status and physical activity did not modify the associations of GI, GL, or rice intake with endometrial cancer, which is consistent with one study [29], but not with several other previous studies [5–7]. On the other hand, we found that the positive association of GI with cancer appeared to be more evident among lean or normal weight women, which is inconsistent with results derived from Western populations [5–7,29], and in particular, in contrast to the report of Augustin *et al* [4], in which a more pronounced association of GI with endometrial cancer was observed in obese women. The biological explanation for our finding is not immediately clear. It has been suggested that a high-GI meal can elicit changes in the IGF system among young and lean people [30]. Whether lean people are more sensitive to a high-GI diet compared with people who are overweight or obese remains to be investigated. The possible modifying effect of BMI on the GI and cancer association, if confirmed, may help to explain the lack of a significant association of endometrial cancer with GI in six of seven studies conducted in Western countries where obesity and overweight are highly prevalent [5–8,10,11,29].

Dietary patterns in China differ substantially from those in Western populations. In Shanghai, for example, rice is the main staple food, and potatoes are usually consumed as a vegetable. In this study, the median intake of raw rice was 250 g/d, which accounted for 79.1% of dietary GL, whereas the median intake of potatoes was only 8.1 g/d, which accounted for only 0.6% of dietary GL. Rice consumption, the top contributor to GL in our study population, was strongly related to increased risk for endometrial cancer, lending support to there being a positive link between GL and cancer risk. The lack of a significant association between intake of tubers and cancer risk may be attributed to the low consumption level.

As with all nutritional epidemiology studies, exposure misclassification is always a concern. In our study, intakes of energy, total carbohydrates, GL, and GI were calculated from a validated FFQ. Although the assessment was found to be valid relative to other self-report instruments [13], misclassification in dietary intake is unavoidable. It has been suggested that obese people tend to underreport dietary exposures (e.g. by about 30% for energy), and the degree of underestimation increases with increasing percentage of body fat [31]. If GL was substantially underestimated among obese women compared with women with normal weight, the association between GL and endometrial cancer would be biased towards null. Lifestyle changes after cancer diagnosis and treatment are another concern, although further analyses by the time interval between cancer diagnosis and interview (<6 months and ≥ 6 months) showed no evidence of a differential effect of GL/GI (data not shown). Our study has high rates of participation for both cases (83%) and controls (74%), however, the refusal rate was slightly higher for controls (21%) than for cases (9%). This difference in response rate would need to be accompanied by very strong selection factors to introduce major biases affecting the magnitude of the associations observed in our study. The general consistency of the results of our case-control study with the results of a number of prospective studies provides support for the validity of our findings.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Our study has a number of strengths. The population-based design, high response rates, and low frequency of hysterectomy in this population have minimized selection bias. The large sample size, extensive dietary information, and unique dietary pattern allowed a comprehensive evaluation of the effect of GI, GL, and a high GI diet on endometrial cancer risk, although the study did not have enough power for some interaction evaluations. Finally, the low rates of estrogen replacement therapy use made it possible to exclude this potential source of confounding.

In summary, the present findings provide additional evidence of the important role played by glycemic response to a diet in risk for endometrial cancer. Our results suggest that maintaining lower intake of foods with a high GI value may reduce the risk of endometrial cancer.

Acknowledgments

We thank Dr. Fan Jin for her contributions in implementing the study and Ms. Bethanie Rammer for her assistance in editing and preparing the manuscript. We also gratefully acknowledge the dedicated efforts of all study participants and research staff of the Shanghai Endometrial Cancer Study. This work was supported by United States Public Health Service (USPHS) grant number R01CA092585 to X.-O. Shu from the US National Cancer Institute.

References

1. 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(1):38–42. DOI: 10.1002/(SICI)1097-0215(19990702)82:1<38::AID-IJC8>3.0.CO;2-Q[pii] [PubMed: 10360818]
2. Livesey G, Taylor R, Hulshof T, Howlett J. Glycemic response and health--a systematic review and meta-analysis: relations between dietary glycemic properties and health outcomes. Am J Clin Nutr. 2008; 87(1):258S–268S. 87/1/258S [pii]. [PubMed: 18175766]
3. Kaaks R, Lukanova A, Kurzer MS. Obesity, endogenous hormones, and endometrial cancer risk: a synthetic review. Cancer Epidemiol Biomarkers Prev. 2002; 11(12):1531–1543. [PubMed: 12496040]
4. Augustin LS, Gallus S, Bosetti C, Levi F, Negri E, Franceschi S, Dal Maso L, Jenkins DJ, Kendall CW, La Vecchia C. Glycemic index and glycemic load in endometrial cancer. Int J Cancer. 2003; 105(3):404–407. DOI: 10.1002/ijc.11089 [PubMed: 12704677]
5. Larsson SC, Friberg E, Wolk A. Carbohydrate intake, glycemic index and glycemic load in relation to risk of endometrial cancer: A prospective study of Swedish women. Int J Cancer. 2007; 120(5): 1103–1107. DOI: 10.1002/ijc.22422 [PubMed: 17131331]
6. Silvera SA, Rohan TE, Jain M, Terry PD, Howe GR, Miller AB. Glycaemic index, glycaemic load and risk of endometrial cancer: a prospective cohort study. Public Health Nutr. 2005; 8(7):912–919. S1368980005001229 [pii]. [PubMed: 16277808]
7. Folsom AR, Demissie Z, Harnack L. Glycemic index, glycemic load, and incidence of endometrial cancer: the Iowa women's health study. Nutr Cancer. 2003; 46(2):119–124. DOI: 10.1207/S15327914NC4602_03 [PubMed: 14690786]
8. Galeone C, Augustin LS, Filomeno M, Malerba S, Zucchetto A, Pelucchi C, Montella M, Talamini R, Franceschi S, La Vecchia C. Dietary glycemic index, glycemic load, and the risk of endometrial cancer: a case-control study and meta-analysis. Eur J Cancer Prev. 2013; 22(1):38–45. DOI: 10.1097/CEJ.0b013e328354d378 [PubMed: 22584216]
9. Nagle CM, Olsen CM, Ibiebele TI, Spurdle AB, Webb PM. Glycemic index, glycemic load and endometrial cancer risk: results from the Australian National Endometrial Cancer study and an updated systematic review and meta-analysis. Eur J Nutr. 2013; 52(2):705–715. DOI: 10.1007/s00394-012-0376-7 [PubMed: 22648201]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

10. Choi Y, Giovannucci E, Lee JE. Glycaemic index and glycaemic load in relation to risk of diabetes-related cancers: a meta-analysis. Br J Nutr. 2012; 108(11):1934–1947. DOI: 10.1017/S0007114512003984S0007114512003984[pii] [PubMed: 23167978]

11. Mulholland HG, Murray LJ, Cardwell CR, Cantwell MM. Dietary glycaemic index, glycaemic load and endometrial and ovarian cancer risk: a systematic review and meta-analysis. Br J Cancer. 2008; 99(3):434–441. DOI: 10.1038/sj.bjc.66044966604496[pii] [PubMed: 18665189]

12. Gnagnarella P, Gandini S, La Vecchia C, Maisonneuve P. Glycemic index, glycemic load, and cancer risk: a meta-analysis. Am J Clin Nutr. 2008; 87(6):1793–1801. 87/6/1793 [pii]. [PubMed: 18541570]

13. Shu XO, Yang G, Jin F, Liu D, Kushi L, Wen W, Gao YT, Zheng W. Validity and reproducibility of the food frequency questionnaire used in the Shanghai Women's Health Study. Eur J Clin Nutr. 2004; 58(1):17–23. DOI: 10.1038/sj.ejcn.16017381601738[pii] [PubMed: 14679362]

14. Yang, Y., Wang, G., Pan, X. Chinese Food Composition 2002. Peking University Medical Press China CDC; 2002.

15. Liu S, Manson JE, Stampfer MJ, Holmes MD, Hu FB, Hankinson SE, Willett WC. Dietary glycemic load assessed by food-frequency questionnaire in relation to plasma high-density-lipoprotein cholesterol and fasting plasma triacylglycerols in postmenopausal women. Am J Clin Nutr. 2001; 73(3):560–566. [PubMed: 11237932]

16. Villegas R, Liu S, Gao YT, Yang G, Li H, Zheng W, Shu XO. Prospective study of dietary carbohydrates, glycemic index, glycemic load, and incidence of type 2 diabetes mellitus in middle-aged Chinese women. Arch Intern Med. 2007; 167(21):2310–2316. 167/21/2310 [pii] . DOI: 10.1001/archinte.167.21.2310 [PubMed: 18039989]

17. Foster-Powell K, Holt SH, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. Am J Clin Nutr. 2002; 76(1):5–56. [PubMed: 12081815]

18. 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(4):779–785. 14/4/779 [pii] . DOI: 10.1158/1055-9965.EPI-04-0665 [PubMed: 15824143]

19. Ainsworth BE, Haskell WL, Whitt MC, Irwin ML, Swartz AM, Strath SJ, O'Brien WL, Bassett DR Jr, Schmitz KH, Emplaincourt PO, Jacobs DR Jr, Leon AS. Compendium of physical activities: an update of activity codes and MET intensities. Med Sci Sports Exerc. 2000; 32(9 Suppl):S498–504. [PubMed: 10993420]

20. Matthews CE, Shu XO, Yang G, Jin F, Ainsworth BE, Liu D, Gao YT, Zheng W. Reproducibility and validity of the Shanghai Women's Health Study physical activity questionnaire. Am J Epidemiol. 2003; 158(11):1114–1122. [PubMed: 14630608]

21. 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; 161(10):939–947. 161/10/939 [pii] . DOI: 10.1093/aje/kwi127 [PubMed: 15870158]

22. Hu FB, Stampfer MJ, Rimm E, Ascherio A, Rosner BA, Spiegelman D, Willett WC. Dietary fat and coronary heart disease: a comparison of approaches for adjusting for total energy intake and modeling repeated dietary measurements. Am J Epidemiol. 1999; 149(6):531–540. [PubMed: 10084242]

23. Willett, W., Stampfer, MJ. Nutritional Epidemiology. Oxford University Press; New York, NY: 1998. Implications of total energy intake for epidemiological analysis.

24. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet. 2004; 363(9403):157–163. S0140-6736(03)15268-3 [pii] . DOI: 10.1016/S0140-6736(03)15268-3 [PubMed: 14726171]

25. Marsh K, Brand-Miller J. The optimal diet for women with polycystic ovary syndrome? Br J Nutr. 2005; 94(2):154–165. S0007114505001674 [pii]. [PubMed: 16115348]

26. Ludwig DS. The glycemic index: physiological mechanisms relating to obesity, diabetes, and cardiovascular disease. JAMA. 2002; 287(18):2414–2423. jsc10297 [pii]. [PubMed: 11988062]

27. Augustin LS, Franceschi S, Jenkins DJ, Kendall CW, La Vecchia C. Glycemic index in chronic disease: a review. Eur J Clin Nutr. 2002; 56(11):1049–1071. DOI: 10.1038/sj.ejcn.1601454 [PubMed: 12428171]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

28. Jenkins DJ, Kendall CW, Augustin LS, Franceschi S, Hamidi M, Marchie A, Jenkins AL, Axelsen M. Glycemic index: overview of implications in health and disease. Am J Clin Nutr. 2002; 76(1): 266S–273S. [PubMed: 12081850]

29. Cust AE, Slimani N, Kaaks R, van Bakel M, Biessy C, Ferrari P, Laville M, Tjonneland A, Olsen A, Overvad K, Lajous M, Clavel-Chapelon F, Boutron-Ruault MC, Linseisen J, Rohrmann S, Nothlings U, Boeing H, Palli D, Sieri S, Panico S, Tumino R, Sacerdote C, Skeie G, Engeset D, Gram IT, Quiros JR, Jakszyn P, Sanchez MJ, Larranaga N, Navarro C, Ardanaz E, Wirfalt E, Berglund G, Lundin E, Hallmans G, Bueno-de-Mesquita HB, Du H, Peeters PH, Bingham S, Khaw KT, Allen NE, Key TJ, Jenab M, Riboli E. Dietary carbohydrates, glycemic index, glycemic load, and endometrial cancer risk within the European Prospective Investigation into Cancer and Nutrition cohort. Am J Epidemiol. 2007; 166(8):912–923. kwm161 [pii] . DOI: 10.1093/aje/kwm161 [PubMed: 17670911]

30. Brand-Miller JC, Liu V, Petocz P, Baxter RC. The glycemic index of foods influences postprandial insulin-like growth factor-binding protein responses in lean young subjects. Am J Clin Nutr. 2005; 82(2):350–354. 82/2/350 [pii]. [PubMed: 16087978]

31. Heitmann BL, Lissner L. Dietary underreporting by obese individuals--is it specific or non-specific? BMJ. 1995; 311(7011):986–989. [PubMed: 7580640]

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

Table 1

Characteristics of controls by quartiles of glycemic load.

Characteristics	Glycemic load quartiles				*P* value
	<171.9	172.0–200.6	200.7–233.7	>233.7	
Dietary data					
Energy intake, mean, kcal/d	1327.0	1617.2	1832.0	2239.0	<0.0001
Carbohydrates, mean, g/d	211.6	265.0	304.4	386.2	<0.0001
Total fat intake, mean, g/d	27.9	31.9	35.4	39.3	<0.0001
Protein, mean, g/d	57.4	67.5	73.8	84.9	<0.0001
Fiber, mean, g/d	10.0	11.1	11.7	13.7	<0.0001
Demographic and lifestyle factors					
Age, mean, yr.	54.4	55.1	54.9	55.8	0.19
Education (%)					
Less than elementary	12.5	11.2	8.3	11.9	
Elementary	11.6	13.2	13.5	13.5	
Middle school	32.3	33.3	43.6	36.3	
High school	29.0	27.1	24.1	27.4	
College or above	14.5	15.2	10.6	10.9	0.23
Income (%; RMB/month per capita)					
<4166.67	24.2	29.1	26.2	36.3	
4166.68–6250.00	25.2	29.1	27.5	23.1	
6250.01–8750.00	23.8	18.9	23.2	22.4	
>8750.00	26.8	22.9	23.2	18.2	0.0035
Occupation (%)					
Professional	25.4	25.1	26.4	24.1	
Clerical	24.4	24.1	21.1	19.5	
Manual laborers	50.2	50.8	52.5	56.4	0.28
Postmenopausal status (%)	58.8	60.4	63.4	70.0	0.0031
Smoking status (%)	6.9	3.6	5.3	5.6	0.89
Alcohol consumption (%)	6.9	3.6	5.3	5.6	0.69
BMI, mean	23.5	23.6	23.8	24.4	0.0018

Characteristics	Glycemic load quartiles				*P* value
	<171.9	172.0–200.6	200.7–233.7	>233.7	
WHR, mean	0.81	0.82	0.82	0.82	0.26
History of diabetes (%)	9.9	7.3	5.6	4.6	0.007
Regular exercise participation (%)	32.0	34.6	31.0	36.3	0.41
Non-occupational activity[a], mean, MET-hrs/d	10.4	10.8	11.0	11.7	0.0020

[a]Including lifestyle activity and exercise.

[b]*P* value: Wilcoxon rank-sum test for numeric variables and χ^2 test for categorical variable.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Author Manuscript

Table 2

Odds ratios (95% confidence intervals) for endometrial cancer by quartiles (Q) of carbohydrate intake in Chinese women, the Shanghai Endometrial Cancer Study, 1997–2003.

	Carbohydrate intake [a]				***P for trend***
	Q1	**Q2**	**Q3**	**Q4**	
Amount of carbohydrate intake (g/day) [b]					
Cases/Controls	274/303	291/303	316/303	318/303	
Age-adjusted OR (95%CI)	1.0	1.1 (0.8–1.3)	1.2 (0.9–1.4)	1.2 (0.9–1.5)	*0.15*
Fully-adjusted OR (95%CI)	1.0	1.0 (0.8–1.3)	1.0 (0.7–1.3)	0.9 (0.6–1.3)	*0.68*
Energy-adjusted carbohydrate intake [c]					
Cases/Controls	328/303	299/303	265/303	307/303	
Age-adjusted OR (95%CI)	1.0	0.9 (0.7–1.1)	0.8 (0.6–1.0)	0.9 (0.8–1.2)	*0.39*
Fully-adjusted OR (95%CI)	1.0	1.0 (0.8–1.2)	0.8 (0.7–1.1)	1.0 (0.8–1.3)	*0.66*
Percentage of energy from carbohydrates					
Cases/Controls	323/303	309/303	300/303	267/303	
Age-adjusted OR (95%CI)	1.0	1.0 (0.8–1.2)	0.9 (0.7–1.2)	0.8 (0.7–1.0)	*0.11*
Fully-adjusted OR (95%CI)	1.0	1.0 (0.8–1.3)	0.9 (0.7–1.2)	0.9 (0.7–1.1)	*0.22*

Fully adjusted OR: adjusted for age (yrs.), per capita income (<4166.67, 4166.68–6250.00, 6250.01–8750.00 and >8750.00 RMB), menopausal status, history of diabetes, non-occupational physical activity (MET-hrs/d, quartiles), and body mass index (quartiles).

[a]Quartile cut points were 241.5, 283.8, and 393.5 (g/d) for amount of carbohydrate intake; −0.055, 0.015, and 0.070 for energy-adjusted carbohydrate intake; and 62.6, 67.5, and 72.1 for percentage of energy from carbohydrates.

[b]Additionally adjusted for energy intake (kcal/d, continuous variable) for fully adjusted OR.

[c]By the energy residual method.

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Table 3

Odds ratios (95% confidence intervals) for endometrial cancer by quartiles (Q) of glycemic load, glycemic index, and high glycemic-index food or food group among Chinese women, the Shanghai Endometrial Cancer Study, 1997–2003.

	Dietary data [a]				*P for trend*
	Q1	**Q2**	**Q3**	**Q4**	
Glycemic load					
Cases/Controls	258/303	297/303	295/303	349/303	
Age-adjusted OR (95%CI)	1.0	1.2 (0.9–1.5)	1.1 (0.9–1.4)	1.4 (1.1–1.7)	*0.01*
OR1 (95%CI)	1.0	1.1 (0.9–1.5)	1.1 (0.8–1.5)	1.3 (0.9–1.9)	*0.21*
OR2 (95%CI) [b]	1.0	1.0 (0.8–1.4)	1.0 (0.7–1.4)	1.1 (0.7–1.7)	*0.83*
Glycemic index					
Cases/Controls	253/303	293/303	333/303	320/303	
Age-adjusted OR (95%CI)	1.0	1.2 (0.9–1.5)	1.3 (1.1–1.7)	1.3 (1.0–1.6)	*0.02*
OR1 (95%CI)	1.0	1.2 (1.0–1.6)	1.4 (1.1–1.8)	1.4 (1.0–1.9)	*0.03*
OR2 (95%CI) [c]	1.0	1.2 (1.0–1.6)	1.4 (1.0–1.9)	1.4 (1.0–2.0)	*0.07*
Staple food items (g/d)					
Cases/Controls	234/305	314/301	308/315	343/291	
Age-adjusted OR (95%CI)	1.0	1.4 (1.1–1.7)	1.3 (1.0–1.6)	1.5 (1.2–1.9)	*0.001*
OR1 (95%CI)	1.0	1.4 (1.1–1.8)	1.3 (1.0–1.7)	1.5 (1.1–2.2)	*0.03*
Rice (g/d)					
Cases/Controls	352/427	372/386	248/226	227/173	
Age-adjusted OR (95%CI)	1.0	1.2 (1.0–1.4)	1.3 (1.1–1.7)	1.6 (1.3–2.1)	*<0.0001*
OR1 (95%CI)	1.0	1.2 (1.0–1.5)	1.4 (1.1–1.9)	1.7 (1.2–2.5)	*0.0014*
Tubers (g/d)					
Cases/Controls	339/303	277/303	306/303	277/303	
Age-adjusted OR (95%CI)	1.0	0.8 (0.7–1.0)	0.9 (0.7–1.1)	0.8 (0.7–1.0)	*0.15*
OR1 (95%CI)	1.0	1.0 (0.8–1.2)	1.1 (0.9–1.4)	1.0 (0.8–1.3)	0.79

[a]Quartile cut points were 171.9, 200.6, and 233.7 for glycemic load; 67.6, 71.2, and 74.5 for glycemic index; 251.6, 299.4, and 350.0 g/d for staple food items; 200, 250, and 300 g/d for rice; and 2.1, 8.3, and 25.8 g/d for tubers.

OR1: adjusted for age (yrs.), per capita income (< 4166.67, 4166.68–6250.00, 6250.01–8750.00 and > 8750.00 RMB), menopausal status, history of diabetes, non-occupational physical activity (MET-hrs/d, quartiles), body mass index (quartiles), energy intake (kcal/d, continuous variable), dietary fiber (g/d, in quartiles), protein (g/d, in quartiles) and fat (g/d, in quartile).

Author Manuscript

OR2:

[b] additionally adjusted for GI;

[c] additionally adjusted for GL.

Author Manuscript
Author Manuscript
Author Manuscript
Author Manuscript

Table 4

Odds ratios (95% confidence intervals) for endometrial cancer by quartiles (Q) of carbohydrate, glycemic load, glycemic index, and rice intake among Chinese women, stratified by BMI, the Shanghai Endometrial Cancer Study, 1997–2003.

		Quartiles[a]						Quartiles[a]					
Dietary items	**Cases/Controls**	**Q1**	**Q2**	**Q3**	**Q4**	***P for trend***	**Cases/Controls**	**Q1**	**Q2**	**Q3**	**Q4**	***P for trend***	***P for interaction***
				BMI < 23						BMI ≥ 23			
Carbohydrates (g/d)	307/524	1.0	0.9(0.6–1.5)	1.0(0.6–1.7)	1.0(0.5–2.0)	*0.97*	883/685	1.0	1.0(0.8–1.4)	1.0(0.7–1.5)	0.9(0.6–1.5)	*0.88*	*0.95*
Glycemic load [b]		1.0	0.9(0.6–1.4)	1.1(0.6–1.8)	1.3(0.7–2.7)	*0.44*		1.0	1.2(0.9–1.7)	1.1(0.8–1.6)	1.3(0.8–2.1)	*0.38*	*0.70*
Glycemic index [b]		1.0	1.9(1.2–3.1)	2.0(1.3–3.3)	1.6(0.9–2.9)	*0.17*		1.0	1.0(0.7–1.3)	1.2(0.8–1.6)	1.3(0.9–1.9)	*0.15*	*0.03*
Rice (g/day) [b]		1.0	1.2(0.8–1.8)	1.6(1.0–2.6)	2.7(1.3–5.4)	*0.008*		1.0	1.2(0.9–1.5)	1.3(0.9–1.8)	1.5(1.0–2.3)	*0.05*	*0.81*
				BMI < 25						BMI ≥ 25			
Carbohydrates (g/d)	572/798	1.0	1.1(0.8–1.5)	1.1(0.8–1.7)	1.0(0.6–1.7)	*0.87*	618/411	1.0	0.9(0.6–1.3)	0.8(0.5–1.3)	0.8(0.5–1.5)	*0.49*	*0.65*
Glycemic load [b]		1.0	1.1(0.8–1.5)	1.2(0.8–1.8)	1.6(1.0–2.7)	*0.06*		1.0	1.1(0.8–1.7)	1.0(0.6–1.5)	1.0(0.6–1.9)	*0.87*	*0.57*
Glycemic index [b]		1.0	1.6(1.1–2.3)	1.9(1.3–2.7)	1.8(1.2–2.8)	*0.0065*		1.0	0.9(0.6–1.3)	1.1(0.7–1.5)	1.0(0.6–1.6)	*0.86*	*0.19*
Rice (g/day) [b]		1.0	1.3(1.0–1.8)	1.9(1.3–2.7)	2.3(1.4–3.8)	*<0.0001*		1.0	1.0(0.7–1.5)	0.9(0.6–1.4)	1.3(0.7–2.2)	*0.66*	*0.10*

[a] Quartile cut points were 241.5, 283.8, and 393.5 (g/d) for amount of carbohydrate intake; 171.9, 200.6, and 233.7 for glycemic load; 67.6, 71.2, and 74.5 for glycemic index; and 200, 250, and 300 g/d for rice.

OR: adjusted for age (yrs.), per capita income (<4166.67, 4166.68–6250.00, 6250.01–8750.00 and >8750.00 RMB), menopausal status, diagnosis of diabetes, non-occupational physical activity (MET-hrs/d, quartiles), energy intake (kcal/d, continuous variable).

[b] Additionally adjusted for dietary intakes of protein (g/d, in quartiles), fiber (g/d, in quartiles), and fat (g/d, in quartiles).