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CONSUMPTION OF SUGARY FOODS AND DRINKS AND RISK OF ENDOMETRIAL CANCER

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Abstract

Consumption of foods high in sugar promotes insulin production, which has been linked to endometrial carcinogenesis. We evaluated the impact of dietary intake of sugary foods and beverages, as well as added sugar and total sugar on endometrial cancer risk in a population-based case-control study, including 424 cases and 398 controls. Participants completed an interview and food frequency questionnaire, and provided self-recorded waist and hip measurements. Women in the highest quartile of added sugar intake had significantly increased endometrial cancer risk (OR=1.84, 95% CI: 1.16–2.92). Among women with waist-to-hip ratio ≥0.85, risk was significantly higher for the highest vs. lowest tertile of added sugar intakes (OR=2.50, 95% CI: 1.38–4.52). The association with added sugar also became stronger when analyses were restricted to never users of hormone replacement therapy (OR: 2.03; 95% CI: 1.27–3.26, for highest vs. lowest tertile). There was little evidence of effect modification by body mass index or physical activity. Given the high prevalence of intake of sugary foods and drinks in Western populations, additional research is warranted to confirm our findings on endometrial cancer.

Keywords

Endometrial neoplasms; diet; sugar; sugary foods; sugary drinks; added sugars

Introduction

Endometrial cancer is the most common gynecologic cancer in the United States, and it is estimated that 47,130 new cases of uterine cancers will be diagnosed in 2012 and about 8,010 of these women will die from the disease (1). Risk is mainly related to reproductive characteristics that affect hormone levels. In particular, high levels of endogenous estrogen unopposed by progesterone increases the stimulation of endometrial epithelial cells providing opportunity for carcinogenesis (2). Unopposed estrogen hormone replacement

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therapy, early onset of menses, nulliparity, and obesity increase endometrial cancer risk by prolonging or increasing estrogen exposure to the endometrium (3). Hyperinsulinemia and diabetes have also been independently associated with increased endometrial cancer risk (3). Consuming foods with high sugar content promotes insulin production and when consumed in great amounts can lead to obesity and ultimately hyperinsulinemia (4). Hence, high sugar consumption may increase endometrial cancer risk by leading to hyperinsulinemia (5, 6). Insulin may influence cancer risk directly and indirectly. First, insulin promotes cellular proliferation and tumor growth by acting directly on endometrial tissue as a mitogenic and antiapoptotic growth factor (7–9). Insulin may also directly improve tumor development via insulin receptors in the endometrium (9). There is evidence that chronic hyperinsulinemia may play a significant role in the onset of ovarian hyperandrogenism, through anovulation and decreased progesterone levels (9). Therefore, a role for sugary food intake in the etiology of endometrial cancer is biologically plausible.

Even with a steady decrease in overall added sugar consumption among Americans older than two years over the past decade (10), mean intakes remain higher than recommended limits (11). Furthermore, one of the recommendations for cancer prevention in the World Cancer Fund International/American Institute for Cancer Research Second Expert Report is that individuals limit their consumption of energy-dense foods and avoid sugary drinks (12).

Total sugars are the sum of both natural and added sugars in the diet (13). Natural sugars, such as fructose or lactose, are found in whole fruit, vegetables, or milk products, which also have nutrients and phytochemicals that are beneficial to one's health (14). On the other hand, added sugars are all caloric sweeteners that have been added to foods or beverages during processing, preparation, and also consumed separately or at the table. Foods with added sugars tend to be high in calories and lacking essential nutrients (14). Examples of added sugars are sucrose (i.e. table sugar), high-fructose corn syrup (HFCS), honey, molasses, and syrups (10, 13, 14). Sucrose and HFCS are both made up of approximately equal amounts of glucose and fructose (10, 15). Sugary foods and beverages are foods that have been processed, prepared, or consumed with caloric sweeteners (14).

While the impact of obesity on invasive endometrial cancer risk is well established, the evidence for the role of individual dietary factors is generally inconsistent (16). Four cohorts (7, 17–19) and 13 case-control studies (20–33) have evaluated individual sugary foods and/or beverages (e.g., "cola containing beverages", "sweets"), with only one study evaluating added sugars from all food sources and cancer risk (19). Overall, the evidence is inconclusive. Hence, the objective of our study was to conduct a comprehensive assessment of the relationship between both total as well as added sugar consumed from sugary foods and drinks and endometrial cancer risk. Furthermore, studying the effects of factors capable of modifying the body's insulin response, such as body mass index (BMI), central obesity, and physical activity, may provide a greater insight into the underlying mechanisms between dietary intake of sugary foods and beverages and endometrial cancer. However, only four studies have considered possible effect modification by insulin-related factors such as diabetes (7, 17), BMI (7, 17, 22, 26), waist-to-hip ratio (WHR) (7), or physical activity (7, 17), with inconclusive results. Hence, the purpose of this study was to evaluate the association between sugary foods and beverages and endometrial cancer risk, and to assess potential effect modification by important factors that impact insulin sensitivity among participants in the EDGE (Estrogens, Diet, Genetics, and Endometrial Cancer) Study.

MATERIALS AND METHODS

Study Population

The EDGE Study has been described in detail elsewhere (34–36). Briefly, the EDGE Study is a population-based case-control study among women older than 21 years, who were able to speak English and/or Spanish, and residents of six contiguous counties in New Jersey (Essex, Union, Morris, Middlesex, Bergen, and Hudson). Women with newly diagnosed, histologically confirmed epithelial endometrial cancer were eligible as cases. Cases were identified between July 1, 2001 and June 30, 2005, through rapid case ascertainment by the New Jersey Cancer Registry and interviewed between January 2002 and April 2006. During this period, 1104 women out of the 1559 potentially eligible women identified were contacted within one year of their diagnosis.

Controls had to meet the same eligibility criteria as cases and were not eligible if they have had a hysterectomy. A commercial research service identified 355 eligible women under 65 years of age via random digit dialing (RDD, stratified by age) of whom 175 completed the interview. Women who were 65 years and older were randomly selected from lists purchased from the Centers for Medicare and Medicaid Services (CMS) and contacted by letter, followed by telephone calls when phone numbers could be located. Sixty-eight (22%) of the 316 women identified completed the interview. Forty percent of those who declined had unknown eligibility. Starting in August 2003, we employed area sampling for controls in randomly selected areas within the six counties. A letter was mailed to households to introduce the study, followed by home visits by interviewers to ascertain eligibility and interest in participating. We initially sought women ages 65 years and over and later included women ages 55 years and over. Of the 524 eligible women identified, 224 (43%) completed the interview. Controls were interviewed between January 2002 and December 2005.

Informed consent was obtained from all participants and this study has been approved by the New Jersey Department of Health and Senior Services, Memorial Sloan-Kettering Cancer Center and University of Medicine and Dentistry of New Jersey (UMDNJ) Robert Wood Johnson Medical School Institutional Review Boards.

Data Collection

Passive approval was obtained from physicians to contact their patients before subjects were invited to participate. Informed consent was obtained before the phone interview by mail. The main questionnaire was administered by phone by trained interviewers to obtain information on several factors, including demographic characteristics, risk factors for endometrial cancer, and other exposures up to a year prior to their diagnosis (or reference date for controls). Factors ascertained included: menstrual history, pregnancy history, a detailed history of exogenous estrogen use (hormone replacement therapy and oral contraceptive use), self-reported height and weight, medical history (diabetes, hypertension, and other conditions), a detailed family history of cancer, and other related exposures. Physical activity, smoking history, and exposure to passive smoking were also assessed. A self-administered food frequency questionnaire and mouthwash sample for DNA extraction and analysis were also collected from participants by mail. We also obtained self-recorded waist and hip measurements with a measuring tape (sent to them with instructions before the interview).

This study used the Block 98.2 Food Frequency Questionnaire (FFQ) (37) to assess usual dietary intake 6 months prior to the case's diagnosis date or the control's date of interview. The FFQ is based on the NHANES (National Health and Nutrition Examination Survey) III dietary recall data and includes 110 food items and questions on frequency of intake and

amount consumed for each food. Pictures were provided to help participants estimate the usual amount of food consumed. This FFQ was shown to have moderate to high validity and reliability (37). Nutrient calculations based on the USDA Nutrient Database for Standard Reference (38) were provided by Berkeley Nutrition Services.

In total, 469 cases and 467 controls completed the main interview. Of these, 424 cases (90.4%) and 398 controls (85.2%) also completed the FFQ. Participants were excluded from the present analysis if they did not complete the FFQ or their menopausal status was unknown or if they were missing other major covariates. Those who were postmenopausal but did not know their age at menopause were included in the analysis. There were no significant differences in age, education, BMI and HRT use between women who returned the FFQ and those who did not.

Processing of Dietary Data

Participants' responses on frequency and portion sizes for sugary foods and beverages were converted to number of servings per day. For most foods, frequency was measured as 'never', 'a few times per year', 'once per month', '2–3 times per month', 'once per week', '2 times per week', '3–4 times per week', '5–6 times per week', and 'everyday'. For a few foods, 'never' and 'a few times per year' were combined into one choice: 'never or a few times per year' and the choice of '2+ times per day' was added. For drinks, portion size was measured as number of cups, glasses, cans or bottles consumed. For food items, portion sizes were measured in teaspoons, tablespoons, ounces, pounds, cups, pieces, patties, bowls or slices. Serving sizes were based on the Reference Amounts Customarily Consumed (RACC) Per Eating Occasion: General Food Supply by the Food and Drug Administration (39). This document provides the amount of food that is usually consumed per eating occasion, and is based on the 1977–1978 and 1987–1988 Nationwide Food Consumption Surveys. We used the FDA's assigned RACC values to guide our assumptions about participants' portion sizes consumed. For example, we assumed that one cookie (RACC=30 grams) is equivalent to one serving. Therefore, participants who reported usually eating one cookie per occasion were assigned as eating one serving for this food item.

Select foods and drinks were converted to number of servings per day to calculate each individual's number of servings of dessert foods, non-dessert foods, sugary drinks and total sugary foods and drinks. Food items included in the calculation of these food groups are listed in Table 2. Total and added sugar intakes (g/day) were calculated separately by multiplying the frequency of consumption of each food by its total/added sugar content per 100 grams of food. Total and added sugar values for all food and drink items were assigned using the USDA Database for the Added Sugars Content of Selected Foods, Release 1(40).

Statistical Analyses

Descriptive statistics for cases and controls were conducted first. For all analyses, statistical significance was considered as p-value less than 0.05. Mean, median, standard errors, and range for nutrient and food groups under consideration were derived and inspected. We computed frequencies to characterize the study population, including age, race, education, oral contraceptive (OC) use, unopposed estrogen hormone replacement therapy (ERT) use, age at onset of menses, parity, body mass index (BMI; weight in kg / height in m^2), diabetes, smoking status, menopausal status. Age-adjusted odds ratios (OR) and 95% confidence interval (CI) were also estimated.

Using ANCOVA, age-adjusted means were calculated to compare mean intake between cases and controls for each of the following food and drink groups: dessert foods, non-

dessert foods, and sugary drinks. Age-adjusted means were also calculated for total sugary foods and drinks, as well as for total sugars and added sugar intakes.

Based on the distribution for controls, quartiles were created for each of the food and drink groups and total and added sugar intakes and frequencies were calculated across the quartiles. Multiple unconditional logistic regression models were used to calculate ORs and 95% CIs adjusted for age and other potential confounders to compare endometrial cancer risk across the quartiles for each of the food and drink groups, total and added sugars, and for % calories from sweets.

Covariates considered in the multiple logistic regression model included age (continuous), education (high school or less, college, graduate school), race (White, Black, Other, Hispanic-any race), age at menarche (>13, 12–13, ≤11), menopausal status (pre- or postmenopausal) and age at menopause for postmenopausal women (<40, 41–54, ≥55, age at menopause unknown), parity (0–1, 2, ≥ 3), OC use (ever vs. never), hormone replacement therapy (HRT) use (never, unopposed estrogen only, any combined HRT), BMI (weight in kg / height in m^2; continuous), smoking status (never, past, current) and pack-years (continuous) for ever smokers, physical activity measured in METs (continuous), fiber intake, and diabetes (yes vs. no). To adjust for total energy intake we used the multivariate nutrient density method (41). Specifically, we calculated density measures for servings of sugary foods and/or drinks per 1,000 kcal of intake, as well as grams of total or added sugars per 1,000 kcal of intake and daily caloric intake was included as a continuous variable in the multivariable models. Tests for trends were derived by assigning to each quartile, the median number of servings of sugary foods and/or beverages per 1,000 kcal or total and added sugar in g/1,000 kcal among controls.

We also explored if women who have risk factors of hyperinsulinemia have higher odds of developing endometrial cancer associated with sugar consumption. We calculated ORs and 95% CIs and used the Wald test to obtain p-values to evaluate if factors like BMI (normal vs. overweight or obese), WHR (<0.85 vs. ≥ 0.85), and physical activity (<median vs. ≥ median, determined by controls) modified endometrial cancer risk across tertiles for total sugary foods and drinks and total and added sugars. Since the number of women with diabetes was small, we repeated the analyses evaluating sugary foods and drinks and total and added sugars, excluding cases and controls diagnosed with diabetes.

RESULTS

Controls tended to be older than cases (mean age was 63.4 vs. 61.6 years, respectively, $p<0.01$). Demographic characteristics for the study population and the distribution of major risk factors for cases and controls are shown in Table 1. Our study population was composed of predominantly white (85.3% and 88.8% for cases and controls, respectively), postmenopausal women. As expected, obesity was strongly associated with endometrial cancer risk while having more children, use of oral contraceptives or any combined HRT, late onset of menses, and current smoking were associated with reduced risk after adjusting for age.

Age-adjusted mean values for sources of sugars are shown in Table 2. Compared to controls, cases had significantly higher total and added sugar intakes and were also more likely to consume breads and condiments with added sugars.

Likewise, in multivariate analyses (Table 3) higher consumption of sugary foods and drinks tended to be associated with increased endometrial cancer risk after adjusting for age and energy intake. Further adjustments for known risk factors for endometrial cancer resulted in attenuation of risk estimates with confidence intervals including one for total sugary foods

and drinks, dessert food, non-dessert foods, and % kcal from sweets. However, a strong association with added sugars persisted. Women in the highest vs. the lowest quartile of added sugars had an OR of 1.84 (95% CI: 1.16–2.92). Further adjustment for diabetes (yes vs. no) or fiber intake (g) did not meaningfully influence results.

Risk of endometrial cancer in relation to sugary foods, sugary drinks, and total and added sugars did not change after repeating multivariate analyses excluding cases and controls diagnosed with diabetes (data not shown). Oral contraceptive use did not appear to influence results either (data not shown). We attempted to evaluated results by HRT use. However, the number of women who ever used unopposed estrogen replacement therapy or combined HRT was too small to evaluate separately. Therefore, we compared results for the overall study population to those in never HRT users. The magnitude of the association was similar for all variables under evaluation (data not shown), except for added sugars (Table 4). Compared to the total study population, risk was much stronger when analyses were restricted to never users of HRT (OR=1.58, 95% CI: 1.00–2.50 and OR=2.03, 95% CI: 1.27–3.26 for the second and third tertiles of added sugar intake, respectively).

Table 4 also shows risk estimates for added sugars, stratified by BMI, waist-to-hip ratio (WHR), and level of physical activity adjusted for major risk factors. There was little evidence of effect modification by any of these factors, with the exception of added sugar by WHR. Specifically, the association between added sugar and endometrial cancer risk appeared to be much stronger among women with central obesity (WHR≥0.85), with an OR of 2.50 (95% CI: 1.38–4.52) for women in the highest tertile of consumption compared to the lowest.

DISCUSSION

In this population-based case-control study we conducted a comprehensive assessment of the relationship between endometrial cancer and sugary foods and drinks, total and added sugar consumption. We found that the consumption of added sugars was associated with increased endometrial cancer risk after adjusting for several major risk factors. Specifically, those who were in the highest category of added sugar intake were approximately 84% more likely to have endometrial cancer. There was also some suggestion of increased risk associated with the consumption of dessert foods, non-dessert foods, total sugars and percent of calories from sweets, although risk estimates were not significant after adjusting for other covariates.

There have been only four population-based case-control studies (22–25) evaluating the effects of sugary foods on endometrial cancer risk and all of them reported null findings for desserts or sweets. To our knowledge, our study is the first population-based case-control study to examine the independent effects of total and added sugars consumption on cancer risk. In a previously published study, also using data from the EDGE Study, we examined the relationship between sugar added to coffee/tea and endometrial cancer risk in the EDGE Study (20). We found endometrial cancer risk more than doubled among women who usually added ≥ 2 teaspoons of sugar/honey per cup of tea compared to women who added none (OR=2.66, 95% CI: 1.42–4.98). There was a suggestion of an adverse effect for women who consumed, daily, ≥ 3 teaspoons of sugar/honey added to coffee or tea vs. women who did not add sugar (OR=1.58, 95% CI: 0.92–2.71).

Consistent with our findings, three large prospective cohort studies found increased risk associated with some aspect of sugar consumption. In the Swedish Mammography Cohort, Friberg et al.(17) reported significantly higher endometrial cancer risk for those who consumed >3 servings/week of “sweet buns and cookies” vs. <0.5 servings/week, at both

baseline (1987) and follow-up (1997) (Quartile 4: Rate Ratio (RR)=1.42, 95% CI:1.15–1.75 and RR=1.72, 95 % CI:1.06–2.78, respectively). Although they did not find an association between soft drinks (yes vs. no) and cancer risk, the authors noted that in Sweden soft drinks are sweetened with sucrose as opposed to high-fructose corn syrup, the predominant caloric sweetener used in soft drinks in the US. Furthermore, their study population has lower levels of sucrose intake in comparison to Americans surveyed by the Third National Health and Nutrition Examination Survey (NHANES III) 1988–1994(42) (17). Friberg et al. also reported significant higher risk associated with increasing sucrose intake (g/day) in both their baseline and follow-up dietary data. In the NIH-AARP Diet and Health Study, Tasevska et al. found greater risk of endometrial cancer associated with the consumption of total sugars, and evidence of increased risk associated with total fructose and sucrose. However, they did not find a relationship between added sugar intake and endometrial cancer risk (19).

In the European Prospective Investigation into Cancer and Nutrition Cohort (EPIC) Study (7), Cust et al. did not find an association between “cakes, pastries, biscuits”, carbonated beverages, and confectionery sugar and endometrial cancer risk, although there was a suggestion of a slight increased risk with total sugar consumption. As in our study, the investigators found a non-significant increase in endometrial cancer risk associated with high level of total sugars intake (g/day) (Quartile 4: RR=1.20, 95% CI: 0.97–1.48). After calibrating their model using 24-hour recall values, they detected significantly higher risk associated with total sugars intake on a continuous scale (per 50 g/day) (RR: 1.36; 95% CI: 1.05–1.76).

Since being overweight or physically inactive is associated with decreased insulin sensitivity and higher insulin levels, it may be possible that overweight or inactive women have greater insulin response to foods with refined sugars (18, 43). To the contrary, a healthful diet, physical activity, weight loss, or the use of insulin-lowering drugs may reduce endometrial cancer risk by improving insulin sensitivity (7, 9, 44) and normalizing plasma androgen levels (9). Folsom et al. suggests that women with diabetes may have lower risk of endometrial cancer if they are more health conscious and keep their diabetes in control, while an increased risk associated with higher glycemic load was seen among non-diabetic women, possibly because their diet may not be as controlled (45). Therefore, we further explored the effects of insulin-modifiers such as diabetes, physical activity, excess body weight and central obesity on the relationship between sugar consumption and endometrial cancer risk. In our study, there were very few women with diabetes (64 cases, 34 controls) and excluding them did not have a major impact on the relationship between cancer risk and any of the exposure variables. Then again, Friberg et al. (17) found that excluding women with diabetes from the analyses did not substantially alter results. Interestingly, WHR, a marker of central obesity, influenced several of our results. In particular, we found a strong association between added sugar intakes for women with a WHR ≥0.85, while we found little evidence of an effect modification by BMI. Clearly, more research is required to further understand potential effect modification by insulin-related factors.

Some limitations of our study must be noted. First, our exposure assessment may have been influenced by recall bias. For example, cases may have systematically underreported consuming unhealthy foods, such as sugary foods and beverages compared to controls, but the opposite is also possible, as cases may have remembered sugar intake better and recall more accurately. Hence, any potential recall bias could be in either direction. However, sugary food and beverage consumption is not broadly known as a risk factor for endometrial cancer and thus, cases may not have purposely recalled incorrectly. As with most population-based case-control studies, our study’s response rates were low and willingness to participate in our study may have been related to subjects’ lifestyle characteristics. For

example, our study participants may live healthier lifestyles and be more enthusiastic about participating in a study on women's health compared to those who refused to participate, which could result in potential selection bias. However, we were unable to compare controls with women who did not participate, as we could not collect information on those who could not be reached or declined to participate in our study. We were, however, able to compare cases who participated to those who did not. We found that our cases were more likely to be younger and be diagnosed with an earlier stage of disease compared to all women diagnosed with endometrial cancer in the same NJ counties (unpublished data from New Jersey State Cancer Registry). However, the distribution of major risk factors, apart from estrogen replacement therapy (ERT), was similar to that of previous reports providing reassurance about the study's validity. With respect to ERT, only a small proportion of cases and controls (less than 10%) used it, and excluding them from our analyses did not alter results.

In summary, we conducted a comprehensive assessment of the relationship between endometrial cancer and sugar consumption, with consideration of factors capable of modifying the body's insulin response. We found that endometrial cancer risk was significantly adversely related to the consumption of added sugars after adjusting for several major risk factors. Furthermore, there was evidence to support that insulin-related risk factors, particularly central obesity, may modify the relationship between sugar consumption and endometrial cancer risk. Our results support the WCRF/AICR 2007 Expert Report recommendations to avoid sugary drinks and the 2010 Dietary Guidelines for Americans that recommend reducing added sugar intake. Our research should be replicated in large cohort studies to further elucidate the role of sugar intake in the etiology of endometrial cancer.

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Table 1

Selected characteristics of women participating in The EDGE Study.

Characteristic	Cases (n=417) n (%)	Controls (n=395) n (%)	p value	Age-Adjusted OR (95% CI)
Education				
High school or less	154 (36.9)	134 (33.9)	0.06	1.00
College	183 (43.9)	158 (40.0)		0.92 (0.66–1.27)
Graduate school	80 (19.2)	103 (26.1)		0.60 (0.41–0.88)
Race/Ethnicity				
White	355 (85.3)	349 (88.8)	0.04	1.00
Black	36 (8.7)	17 (4.3)		1.96 (1.08–3.57)
Other	10 (2.4)	16 (4.1)		0.54 (0.24–1.21)
Hispanic (any race)	15 (3.6)	11 (2.8)		1.14 (0.51–2.54)
Parity				
0–1	147 (35.3)	92 (23.3)	<0.01	1.00
2	142 (34.1)	140 (35.4)		0.64 (0.45–0.90)
≥3	128 (30.7)	163 (41.3)		0.53 (0.37–0.76)
Oral Contraceptive Use				
Never	224 (53.7)	199 (50.4)	0.34	1.00
Ever	193 (46.3)	196 (49.6)		0.69 (0.51–0.93)
HRT Use				
Never	335 (80.3)	291 (73.7)	0.02	1.00
Unopposed E only	34 (8.2)	31 (7.9)		0.97 (0.58–1.63)
Any combined HRT	48 (11.5)	73 (18.5)		0.54 (0.36–0.81)
Age at Menarche				
>13	74 (17.8)	102 (25.9)	0.02	0.66 (0.46–0.95)
12–13	233 (56.0)	198 (50.3)		1.00
≤11	109 (26.2)	94 (23.9)		0.93 (0.66–1.31)
Menopause				
Premenopausal	59 (14.2)	48 (12.2)	0.92	
Postmenopausal	358 (85.9)	347 (87.9)		
Age at menopause				
<40	13 (3.1)	12 (3.0)		0.97 (0.43–2.21)
41–54	254 (60.9)	243 (61.5)		1.00
≥55	41 (9.8)	39 (9.9)		1.11 (0.68–1.80)
Unknown	50 (12.0)	53 (13.4)		0.91 (0.59–1.40)
BMI				
Normal (<25)	105 (25.2)	189 (47.9)	<0.01	1.00
Overweight (25–29.9)	121 (29.0)	119 (30.1)		1.93 (1.36–2.75)
Obese (30–34.9)	68 (16.3)	62 (15.7)		2.02 (1.32–3.08)
Very obese (≥35)	123 (29.5)	25 (6.3)		8.47 (5.16–13.89)
Smoking status			0.24	
Never	231 (55.4)	207 (52.7)		1.00

Characteristic	Cases (n=417) n (%)	Controls (n=395) n (%)	p value	Age-Adjusted OR (95% CI)
Past	159 (38.1)	148 (37.7)		0.97 (0.72–1.30)
Current	27 (6.5)	38 (9.7)		0.58 (0.34–0.98)

Table 2

Age-adjusted means (± SE) for sources of sugars among women in The EDGE Study.

Sources of Sugars	Cases (n=417)	Controls (n=395)	*p*
Total Sugary Foods & Drinks (servings/1000 kcal)	4.79 (0.07)	4.61 (0.07)	0.02
Dessert Foods (servings/1000 kcal)	0.93 (0.04)	0.83 (0.05)	0.12
Doughnuts, Danish pastry	0.05 (0.00)	0.04 (0.00)	0.05
Cakes, sweet rolls, coffee cakes	0.03 (0.00)	0.03 (0.00)	0.19
Cookies	0.42 (0.03)	0.39 (0.03)	<0.01
Ice cream	0.06 (0.00)	0.05 (0.00)	0.16
Pumpkin pie, sweet potato pie	0.01 (0.00)	0.01 (0.00)	0.72
Other pies or cobbler	0.02 (0.00)	0.02 (0.00)	0.03
Chocolate candy, candy bars	0.08 (0.01)	0.07 (0.01)	0.18
Other candy, not chocolate	0.29 (0.03)	0.24 (0.03)	0.85
Non-Dessert Foods (servings/1000 kcal)	3.86 (0.06)	3.78 (0.06)	0.10
Canned fruit, dried fruits	0.04 (0.00)	0.05 (0.00)	0.02
Pancakes, waffles, French toast, Pop Tarts	0.07 (0.01)	0.07 (0.01)	0.95
Breakfast bars, granola bars, Power bars	0.02 (0.01)	0.03 (0.01)	<0.01
Cooked cereals	0.10 (0.01)	0.11 (0.01)	<0.01
Cold cereals	0.17 (0.01)	0.18 (0.01)	0.33
Yogurt/Frozen Yogurt	0.07 (0.01)	0.08 (0.01)	0.33
Breads	0.84 (0.03)	0.80 (0.03)	<0.01
Soups	0.13 (0.01)	0.11 (0.01)	0.01
Jelly, jam, or syrup	0.16 (0.01)	0.15 (0.01)	<0.01
Other condiments	1.56 (0.04)	1.50 (0.04)	0.04
Sugary Drinks (servings/1000 kcal)	0.33 (0.02)	0.25 (0.02)	0.05
Drinks with added vitamin C	0.01 (0.00)	0.01 (0.01)	0.38
Drinks with some fruit juices	0.02 (0.01)	0.01 (0.01)	0.43
Regular soft drinks or bottled drinks	0.11 (0.01)	0.09 (0.01)	0.04
Total Sugars (g/1000 kcal)	65.95 (1.18)	62.78 (1.21)	<0.01
Added Sugars(g/1000 kcal)	30.58 (0.80)	27.28 (0.82)	<0.01

SE: Standard Error

Table 3

Sources of sugar and endometrial cancer risk in The EDGE Study.

Sources of Sugar	Cases (n=417)	Controls (n=395)	OR1	95% CI	OR2	95% CI
Total Sugary Foods & Drinks (servings/1000 kcal)						
(<3.90)	73 (17.5)	99 (25.1)	1.00		1.00	
(3.90–4.74)	96 (23.0)	99 (25.1)	1.32	(0.87–2.00)	1.38	(0.86–2.19)
(4.75–5.76)	135 (32.4)	98 (24.8)	1.88	(1.26–2.82)	1.46	(0.93–2.29)
(>5.76)	113 (27.1)	99 (25.1)	1.66	(1.10–2.51)	1.38	(0.87–2.20)
p trend				<0.01		0.22
Dessert Foods (servings/1000 kcal)						
(<0.25)	94 (22.5)	100 (25.3)	1.00		1.00	
(0.25–0.52)	77 (18.5)	97 (24.6)	0.85	(0.56–1.29)	0.77	(0.49–1.23)
(0.53–1.08)	112 (26.9)	100 (25.3)	1.19	(0.80–1.76)	1.10	(0.70–1.72)
(>1.08)	134 (32.1)	98 (24.8)	1.48	(0.99–2.20)	1.29	(0.83–2.01)
p trend				0.01		0.07
Non-Dessert Foods (servings/1000 kcal)						
(<2.92)	80 (19.2)	99 (25.1)	1.00		1.00	
(2.92–3.69)	122 (29.3)	98 (24.8)	1.61	(1.08–2.41)	1.45	(0.93–2.27)
(3.70–4.46)	102 (24.5)	99 (25.1)	1.31	(0.87–1.97)	1.21	(0.77–1.91)
(>4.46)	113 (27.1)	99 (25.1)	1.52	(1.01–2.29)	1.17	(0.74–1.84)
p trend				0.37		0.80
Sugary Drinks (servings/1000 kcal)						
(<0.02)	88 (21.1)	98 (24.8)	1.00		1.00	
(0.02–0.09)	109 (26.1)	99 (25.1)	1.22	(0.82–1.83)	1.29	(0.83–2.00)
(0.10–0.33)	94 (22.5)	100 (25.3)	1.01	(0.67–1.52)	1.07	(0.67–1.69)
(>0.33)	126 (30.2)	98 (24.8)	1.42	(0.96–2.11)	1.48	(0.94–2.33)
p trend				0.11		0.14
Total Sugars (g/1000 kcal)						
(<46.54)	95 (22.8)	98 (24.8)	1.00		1.00	
(46.54–60.68)	99 (23.7)	100 (25.3)	1.05	(0.70–1.56)	1.25	(0.80–1.97)
(60.69–78.55)	108 (25.9)	99 (25.1)	1.21	(0.82–1.81)	1.28	(0.82–1.99)
(>78.55)	115 (27.6)	98 (24.8)	1.36	(0.91–2.04)	1.43	(0.91–2.27)

Sources of Sugar	Cases (n=417)	Controls (n=395)	OR1	95% CI	OR2	95% CI
p trend				0.09		0.15
Added Sugars (g/1000 kcal)						
(<16.27)	73 (17.5)	99 (25.1)	1.00		1.00	
(16.27–24.06)	108 (25.9)	98 (24.8)	1.61	(1.06–2.44)	1.47	(0.92–2.33)
(24.07–34.16)	99 (23.7)	100 (25.3)	1.35	(0.89–2.05)	1.27	(0.80–2.02)
(>34.16)	137 (32.9)	98 (24.8)	1.94	(1.29–2.92)	1.84	(1.16–2.92)
p trend				<0.01		0.02
% Kcal from sweets						
(<6.50)	79 (18.9)	95 (24.1)	1.00		1.00	
(6.50–11.50)	91 (21.8)	100 (25.3)	1.09	(0.72–1.65)	1.16	(0.73–1.85)
(11.51–17.90)	109 (26.1)	100 (25.3)	1.27	(0.84–1.92)	1.22	(0.78–1.92)
(>17.90)	138 (33.1)	100 (25.3)	1.62	(1.08–2.43)	1.49	(0.94–2.35)
p trend				0.01		0.08

OR: Odds Ratio, CI: Confidence Interval

OR1: adjusted for age (continuous), energy intake (continuous)

OR2: additionally adjusted for education (high school or less, college, graduate school), race (White, Black, Other, Hispanic), age at menarche (continuous), menopausal status (premenopausal, postmenopausal) and age at menopause for postmenopausal women (<40, 42–54, ≥ 55, unknown), parity (0–1, 2, 3–4), oral contraceptive use (ever, never), HRT use (never, unopposed estrogen only, any combined HRT), BMI (continuous), smoking status (never, past, current) and pack-years for ever smokers (continuous), physical activity (METs for reported average hours per week of moderate or strenuous recreational activities). Further adjustment for diabetes (no, yes), fiber intake (g), or date of interview did not essentially change risk estimates.

Table 4

Consumption of added sugars and endometrial cancer risk by selected characteristics in The EDGE Study.

Sources of Sugar	Cases/Controls	Tertile 1	Tertile 2 OR* (95% CI)	Tertile 3 OR* (95% CI)1	*p* for heterogeneity
Added sugars (g/1000 kcal)	(Tertile Cutpoints)	(<19.92)	(19.92–32.24)	(>32.24)	
Total population	417/395	1.00	1.17 (0.80–1.72)	1.62 (1.09–2.42)	
BMI (kg/m^2)					
<25	105/189	1.00	0.98 (0.49–1.96)	1.79 (0.90–3.58)	0.71
≥ 25	312/206	1.00	1.32 (0.81–2.14)	1.75 (1.04–2.95)	
WHR					
<0.85	174/208	1.00	0.91 (0.52–1.59)	1.29 (0.70–2.36)	0.18
≥0.85	232/181	1.00	1.83 (1.01–3.30)	2.50 (1.38–4.52)	
Physically activity (METs)					
<12,2872.5	261/196	1.00	1.08 (0.63–1.88)	1.48 (0.86–2.55)	0.86
≥12,2872.5	154/197	1.00	1.36 (0.76–2.45)	1.64 (0.87–3.08)	
No HRT use	335/291	1.00	1.58 (1.00–2.50)	2.03 (1.27–3.26)	

OR: Odds Ratio, CI: Confidence Interval, WHR: waist-to-hip ratio

OR*: adjusted for age (continuous), energy intake (continuous), education (high school or less, college, graduate school), race (White, Black, Other, Hispanic), age at menarche (continuous), menopausal status (premenopausal, postmenopausal) and age at menopause for postmenopausal women (<40, 42–54, ≥ 55, unknown), parity (0–1, 2, 3–4), oral contraceptive use (ever, never), HRT use (never, unopposed estrogen only, any combined HRT), BMI (continuous), smoking status (never, past, current) and pack-years for ever smokers (continuous), physical activity (METs for reported average hours per week of moderate or strenuous recreational activities), and diabetes.