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# Intakes of Selected Nutrients and Food Groups and Risk of Ovarian Cancer

**Susan E. McCann, Kirsten B. Moysich, and Curtis Mettlin**

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***Abstract:*** *In a hospital-based case-control study, we examined dietary intakes of selected nutrients and food groups and ovarian cancer risk among 496 women with primary, histologically confirmed epithelial ovarian cancer and 1,425 women with nonneoplastic diagnoses, ages 20–87 years, admitted to Roswell Park Cancer Institute between 1982 and 1998. Data on diet and other relevant risk factors in the few years before admission were collected with a self-administered questionnaire. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by unconditional logistic regression adjusting for age, education, region of residence, regularity of menstruation, family history of ovarian cancer, parity, age at menarche, oral contraceptive use, and energy intake. Women in the highest vs. the lowest quartile of total energy had a weak increase in risk (OR = 1.25, 95% CI = 0.90–1.73). Significantly reduced risks were associated with higher intakes of dietary fiber (OR = 0.57, 95% CI = 0.38–0.87), vitamin A (OR = 0.66, 95% CI = 0.45–0.98), carotenoid (OR = 0.64, 95% CI = 0.43–0.93), vitamin E (OR = 0.58, 95% CI = 0.38–0.88), β-carotene (OR = 0.68, 95% CI = 0.46–0.98), and total fruit and vegetable intake (OR = 0.62, 95% CI = 0.42–0.92). Our findings suggest that a diet high in plant foods may be important in reducing risk of ovarian cancer.*

## Introduction

Ovarian cancer is an important cause of morbidity and mortality among women. Over 25,000 new cases were estimated in 1999, with >14,000 estimated deaths (1). The disease is difficult to detect and often quite advanced by diagnosis. The etiology of ovarian cancer has not been clearly elucidated, but risk factors tend to be related to those affecting hormonal and reproductive events. Higher parity and oral contraceptive use have been associated with reduced risks (2). Putative mechanisms for ovarian cancer related to hormonal factors are excessive levels of circulating gonadotropins associated with lower parity and decreased number of ovulatory cycles from higher parity, resulting in reduced mitotic events in the ovary (2).

Diet could contribute to the etiology of ovarian cancer through modulation of the endogenous hormonal milieu (3–13) or through antioxidant and anticarcinogenic mechanisms (14). The relationship between nutrient and food intake and ovarian cancer has been addressed in case-control and prospective designs, although the results have been inconclusive. In general, somewhat increased risks have been reported for higher intakes of total fat and animal fat, cholesterol and lactose intakes (15–17), and higher intakes of meat, eggs, and whole milk (17–19). Conversely, inverse associations have been reported for fiber, vitamin A, β-carotene (20–22), and fruit and vegetable intakes (15–17).

Beginning in 1982, all individuals admitted to Roswell Park Cancer Institute (RPCI), a comprehensive cancer center in Western New York, were asked to complete a comprehensive epidemiological questionnaire that included reproductive and medical histories, family history of cancer, occupational and environmental exposures, tobacco and alcohol consumption, and diet. Since 1982, >40,000 patients with cancer and noncancer diagnoses have completed the questionnaire. Among these, >500 women were diagnosed with ovarian cancer, providing a unique opportunity to investigate the impact of diet on risk of ovarian cancer.

## Methods

### Subjects

The study population included women admitted to RPCI between 1982 and 1998 who agreed to complete a comprehensive epidemiological questionnaire. Informed consent was obtained from all participants. Only women with complete data for the present analyses were included. Cases were 496 women with primary, incident epithelial ovarian cancer, identified from the RPCI tumor registry and diagnostic index. Cases were predominantly Caucasian (98%) and ranged in age between 20 and 87 years. Controls included 1,425

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women who received medical services at RPCI for nonneoplastic conditions, randomly selected from a pool of 5,700 eligible women and frequency matched to the cases by five-year age intervals. The most frequently utilized services for the control patients included the breast clinic (28%), gynecology clinic (17%), surgery (15%), and dermatology clinic (11%). Among the control women, nonneoplastic diagnoses were distributed among the following disease categories: circulatory system (21%), respiratory system (18%), digestive system (16%), musculoskeletal system and connective tissue (12%), endocrine disorder (11%), central nervous system (6%), and other (16%). Similar to cases, women in the control group were predominantly Caucasian and ranged in age between 25 and 90 years.

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### Questionnaire

All participants agreed to complete the Patient Epidemiology Data System (PEDS) questionnaire, which is offered to all new patients as part of the admission process and is completed by ~50% of new patients within three months of diagnosis. The self-administered 16-page instrument covers information on reproductive and medical histories, family history of cancer, occupational and environmental exposures, tobacco and alcohol consumption, and diet.

Diet in the few years before diagnosis (or admission for controls) was queried using a 44-item food frequency questionnaire (FFQ) and did not include information regarding portion size. The five response categories range from never to five to seven times per week. The questionnaire was designed to provide an assessment of intakes of fruits and vegetables, cruciferous vegetables, and foods providing good sources of vitamins A, C, and E, fat, and fiber (23). Foods included on the questionnaire were chosen to provide a profile for each respondent for these nutrients. The foods were selected from data from a detailed diet interview, lasting ~2.5 hours, with each of 282 healthy individuals, participants in the Western New York (WNY) Diet Study I (1975–86). The interview included detailed questions regarding frequency of consumption, portion size, seasonality of intake, and preparation methods for 140 foods. From the food frequency data, an index of nutrient intake was calculated. Multiple linear regression models were then calculated, with nutrient index as the dependent variable and intake of individual foods as the independent variables to obtain the list of foods that explained the largest amount of variance for each nutrient. Although brief, the resultant 44-item food list constituted those foods most highly correlated with the nutrient profiles in question and explained 90% of the total variability in ingestion of vitamins A, C, and E, fat, and dietary fiber (23).

Because of the brevity of the FFQ, nutrient intake was calculated using regression weights derived from the process used to obtain the food list included on the questionnaire. The gender-specific regression weights were computed using dietary data from 1,475 male and 780 female controls, participants of the WNY Diet Study I (1975–86). First, nutrients were computed for the WNY Diet Study using 140 foods, reported frequency of consumption, portion size, cooking method, seasonality, and US Department of Agriculture food composition values. With use of the foods in the WNY Diet Study that represent the 44 foods included on the shorter questionnaire, multiple linear regression models were calculated with each nutrient as the dependent variable and the 44 foods as the independent variables. The resulting regression coefficient for each food and nutrient was then multiplied by the frequency of use reported on the PEDS FFQ summed across foods to obtain an index of each nutrient. Regression weights were available for calculation of mean daily intakes of energy, protein, carbohydrates, total fat, saturated fat, monounsaturated fat, polyunsaturated fat, animal and vegetable fat, cholesterol, dietary fiber, vitamins A, C, and E, retinol, total carotenoids, α-carotene, β-carotene, cryptoxanthin, lutein + zeaxanthin, and lycopene.

In addition to investigating risk of ovarian cancer with nutrient intake, risk associated with monthly frequency of use of several food groups was of interest. Because the FFQ was limited to 44 food items (predominantly fruits and vegetables), we examined the following food groups only: fruits and fruit juices, vegetables, total fruits and vegetables, and meats, categorized according to US Department of Agriculture classification definitions. We were unable to examine frequency of use of dairy products, breads and cereals, or snacks and sweets, inasmuch as these items were not included on the questionnaire.

### Statistical Analyses

Descriptive analyses included Student's *t*-tests of means for cases and controls for continuous variables, and $\chi^2$ tests for categorical variables. For estimation of risk associated with each nutrient, daily nutrient intake was divided into quartiles on the basis of the intake distribution of the controls. Risk of ovarian cancer in each quartile relative to the lowest (referent) quartile of nutrient intake was estimated by odds ratios (ORs) and 95% confidence intervals (CIs) calculated with unconditional logistic regression. ORs were adjusted for potential confounders, including age, education, region of residence, age at menarche, parity, oral contraceptive use, presence of irregular menses, family history of ovarian cancer, and total energy intake. Covariates were included in the final regression model only if they were established risk factors in these data or changed the observed risk estimates by ≥15%.

Analyses of risk associated with specific food groups were conducted in a similar manner. Monthly frequency of use of each group was divided into quartiles on the basis of the intake distribution of the controls. ORs were adjusted for the same covariates as for nutrient intake, with the exception of total energy. To account for differences in diet composition, each food group was further adjusted for monthly frequency of use of the remaining major food groups. Tests for trend for each nutrient and food group were computed from

the $P$ value (2-tailed) of the logistic regression of the continuous nutrient or food group variable within the specified models.

## Results

The descriptive characteristics of the ovarian cancer cases and controls are shown in Table 1. Consistent with the literature, women with ovarian cancer tended to have a later age at first pregnancy, be nulliparous, be less likely to have breast-fed, be less likely to have used oral contraceptives or have a tubal ligation, be less likely to have regular menstrual cycles, and be more likely to have a family history of ovarian cancer than women without ovarian cancer. Cases were also less likely than controls to reside in Western New York. Age at menarche did not differ for women with and without ovarian cancer.

**Table 1.** Descriptive Characteristics of Ovarian Cancer Cases and Hospital Controls: Roswell Park Cancer Institute, Buffalo, NY (1982–96)[a]

| | Cases ($n$ = 496) | Controls ($n$ = 1,425) |
|---|---|---|
| | *Mean ± SD* | |
| Age, yr | 55.1 ± 13.4 | 54.7 ± 13.6 |
| Age at menarche, yr | 13.1 ± 5.7 | 13.2 ± 6.2 |
| Age at 1st pregnancy, yr | 23.2 ± 4.8* | 22.7 ± 5.1 |
| | *Number (%)* | |
| Education | | |
| Up to high school | 258 (52.0) | 781 (54.8) |
| College | 238 (48.0) | 644 (45.2) |
| Place of residence | | |
| Western New York | 234 (47.2)† | 1200 (84.2) |
| Outside Western New York | 262 (52.8) | 225 (15.8) |
| Tubal ligation | | |
| Yes | 67 (13.5)† | 253 (17.8) |
| No | 429 (86.5) | 1172 (82.2) |
| Oral contraceptive use | | |
| Ever | 158 (31.9)† | 494 (34.7) |
| Never | 338 (68.1) | 931 (65.3) |
| Regularity of menses | | |
| Regular | 432 (87.1)† | 1154 (81.0) |
| Irregular | 64 (12.9) | 271 (19.0) |
| Parity | | |
| Nulliparous | 110 (22.2)† | 255 (17.9) |
| 1–2 | 180 (36.3) | 503 (53.3) |
| 3–4 | 168 (33.9) | 496 (34.8) |
| ≥5 | 38 (7.7) | 171 (12.0) |
| Breast feeding | | |
| Never | 311 (64.0)† | 789 (56.6) |
| Ever | 175 (36.0) | 605 (43.4) |
| Family history of ovarian cancer | | |
| No | 460 (92.7)† | 1377 (96.6) |
| Yes | 36 (7.3) | 48 (3.4) |

*a:* Statistical significance is as follows: *, $p < 0.05$ ($t$-test); †, $p < 0.05$ ($\chi^2$ test).

Risk of ovarian cancer associated with mean daily energy and macronutrient intake is shown in Table 2. Compared with women in the lowest quartile of intake, women in the highest quartile of total energy had a weak, but statistically nonsignificant, increase in risk (OR = 1.25, 95% CI = 0.90–1.73). Risk was not related to daily intakes of protein, carbohydrates, total fat, or any fat component in these data, although we observed a borderline statistically significant trend in increasing risk associated with fat from animal sources ($p$ = 0.05).

Risk of ovarian cancer associated with mean daily micronutrient intake is shown in Table 3. We observed reductions in risk of ~30–40% for women in the highest vs. lowest quartiles of dietary fiber (OR = 0.57, 95% CI = 0.38–0.87), total vitamin A (OR = 0.66, 95% CI = 0.45–0.98), total carotenoids (OR = 0.64, 95% CI = 0.43–0.93), vitamin E (OR = 0.58, 95% CI = 0.38–0.88), and β-carotene (OR = 0.68, 95% CI = 0.46–0.98). Somewhat weaker reductions in risk were also observed for vitamin C (OR = 0.69, 95% CI = 0.47–1.03), retinol (OR = 0.71, 95% CI = 0.48–1.04), α-carotene (OR = 0.75, 95% CI = 0.53–1.06), lycopene (OR = 0.81, 95% CI = 0.57–1.15), and lutein + zeaxanthin (OR = 0.76, 95% CI = 0.52–1.10), with vitamin C and lutein + zeaxanthin exhibiting statistically significant trends for reduced risks associated with increasing intake ($p$ = 0.02).

Consistent with the reduced risks observed for the micronutrients, as shown in Table 4, risk of ovarian cancer was reduced by ~40% for women in the highest vs. the lowest quartile of total fruit and vegetable intake (OR = 0.62, 95% CI = 0.42–0.92). Although risks were reduced for women in the highest quartiles of fruits (OR = 0.85, 95% CI = 0.59–1.21) and vegetables (OR = 0.76, 95% CI = 0.52–1.10) examined separately, there did not seem to be a significant improvement in contribution to risk reduction by either individual group. Risk was not related to monthly frequency of meat consumption (OR = 1.17, 95% CI = 0.80–1.71).

## Discussion

Relatively little is known concerning the etiology of ovarian cancer, although hormonal exposures appear to be important (2). There have been few investigations of the impact of food and nutrient intake on ovarian cancer risk, but these, in general, support a protective effect of diets higher in fruits and vegetables, as well as nutrients commonly associated with these foods, such as vitamin C, dietary fiber, and β-carotene (15–17,20–22), and a risk-elevating effect for foods from animal sources, fat, and cholesterol (15–19). Our findings confirm previously reported associations of reduced ovarian cancer risks with vitamin C, dietary fiber, and β-carotene, although we observed no increases in risk associated with any nutrient or food group. Several mechanisms could account for our findings. Vitamins C and E and several of the carotenoids have been shown to be potent antioxidants and, therefore, could affect cancer risk. Diet composition can affect steroid hormone levels, and, therefore, may affect

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**Table 2.** ORs and 95% CIs for Risk of Ovarian Cancer With Daily Macronutrient Intake: Roswell Park Cancer Institute, Buffalo, NY (1982–96)[a]

| | *n* | | OR | *P* Value |
|---|---|---|---|---|
| | Cases | Controls | (95% CI) | for Trend |
| Energy | | | | |
| Q1 (≤1,346 kcal) | 102 | 358 | 1.00 | 0.45 |
| Q2 (1,347–1,754 kcal) | 140 | 354 | 1.26 (0.92–1.73) | |
| Q3 (1,755–2,256 kcal) | 128 | 361 | 1.17 (0.85–1.62) | |
| Q4 (>2,256 kcal) | 126 | 352 | 1.25 (0.90–1.73) | |
| Protein[b] | | | | |
| Q1 (≤56 g) | 109 | 357 | 1.00 | 0.16 |
| Q2 (57–76 g) | 129 | 359 | 1.08 (0.77–1.51) | |
| Q3 (77–102 g) | 129 | 361 | 1.10 (0.74–1.61) | |
| Q4 (>102 g) | 129 | 348 | 1.20 (0.69–2.08) | |
| Carbohydrates[c] | | | | |
| Q1 (≤167 g) | 108 | 354 | 1.00 | 0.81 |
| Q2 (168–216 g) | 142 | 354 | 1.10 (0.78–1.57) | |
| Q3 (217–273 g) | 124 | 366 | 0.95 (0.62–1.44) | |
| Q4 (>273 g) | 122 | 351 | 0.86 (0.47–1.59) | |
| Total fat[d] | | | | |
| Q1 (≤49 g) | 109 | 355 | 1.00 | 0.11 |
| Q2 (50–67 g) | 131 | 362 | 1.17 (0.83–1.64) | |
| Q3 (68–89 g) | 127 | 360 | 1.22 (0.82–1.80) | |
| Q4 (>90 g) | 129 | 348 | 1.48 (0.85–2.60) | |
| Fat from animal sources[e] | | | | |
| Q1 (≤34 g) | 111 | 359 | 1.00 | 0.05 |
| Q2 (35–49 g) | 132 | 360 | 1.16 (0.83–1.62) | |
| Q3 (50–68 g) | 124 | 357 | 1.18 (0.80–1.73) | |
| Q4 (>68 g) | 129 | 349 | 1.34 (0.78–2.32) | |
| Fat from vegetable sources[e] | | | | |
| Q1 (≤14 g) | 117 | 356 | 1.00 | 0.68 |
| Q2 (15–17 g) | 131 | 352 | 1.10 (0.80–1.52) | |
| Q3 (18–22 g) | 123 | 360 | 1.01 (0.72–1.43) | |
| Q4 (>22 g) | 125 | 357 | 0.90 (0.60–1.34) | |
| Saturated fat[e] | | | | |
| Q1 (≤16 g) | 112 | 357 | 1.00 | 0.70 |
| Q2 (17–24 g) | 122 | 361 | 1.06 (0.76–1.49) | |
| Q3 (25–34 g) | 129 | 359 | 1.22 (0.8–1.79) | |
| Q4 (>34 g) | 133 | 348 | 1.36 (0.79–2.35) | |

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**Table 2.** *(Continued)*

| | *n* | | OR (95% CI) | *P* Value for Trend |
|---|---|---|---|---|
| | Cases | Controls | | |
| Monounsaturated fat[e] | | | | |
| Q1 (≤15 g) | 109 | 358 | 1.00 | 0.30 |
| Q2 (16–21 g) | 128 | 361 | 1.18 (0.84–1.65) | |
| Q3 (22–28 g) | 123 | 354 | 1.22 (0.82–1.80) | |
| Q4 (>28 g) | 136 | 352 | 1.50 (0.87–2.61) | |
| Polyunsaturated fat[e] | | | | |
| Q1 (≤8 g) | 115 | 362 | 1.00 | 0.40 |
| Q2 (9–10 g) | 131 | 351 | 1.17 (0.84–1.61) | |
| Q3 (11–13 g) | 127 | 360 | 1.05 (0.74–1.49) | |
| Q4 (<13 g) | 123 | 352 | 0.92 (0.60–1.42) | |

*a:* Q = quartile, adjusted for age, education, region of residence, regularity of menstruation, family history of ovarian cancer, parity, age at menarche, and oral contraceptive use. OR, odds ratio; CI, confidence interval.
*b:* Further adjusted for carbohydrates and fat.
*c:* Further adjusted for protein and fat.
*d:* Further adjusted for carbohydrates and protein.
*e:* Further adjusted for total fat.

**Table 3.** ORs and 95% CIs for Risk of Ovarian Cancer With Daily Micronutrient Intake: Roswell Park Cancer Institute, Buffalo, NY (1982–96)

| | *n* | | OR[a] (95% CI) | *P* Value for Trend |
|---|---|---|---|---|
| | Cases | Controls | | |
| Cholesterol | | | | |
| Q1 (≤ 229 mg) | 120 | 355 | 1.00 | 0.51 |
| Q2 (230–323 mg) | 129 | 364 | 0.88 (0.64–1.22) | |
| Q3 (324–460 mg) | 117 | 356 | 0.86 (0.60–1.23) | |
| Q4 (>460 mg) | 130 | 350 | 0.99 (0.63–1.55) | |
| Dietary fiber | | | | |
| Q1 (≤16 g) | 117 | 350 | 1.00 | 0.03 |
| Q2 (17–22 g) | 141 | 359 | 1.06 (0.77–1.45) | |
| Q3 (23–30 g) | 137 | 362 | 0.85 (0.60–1.19) | |
| Q4 (>30 g) | 101 | 354 | 0.57 (0.38–0.87) | |
| Vitamin C | | | | |
| Q1 (≤112 mg) | 111 | 351 | 1.00 | 0.02 |
| Q2 (113–173 mg) | 136 | 354 | 1.14 (0.83–1.58) | |
| Q3 (174–250 mg) | 153 | 360 | 1.12 (0.80–1.56) | |
| Q4 (>250 mg) | 96 | 360 | 0.69 (0.47–1.03) | |

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**Table 3.** *(Continued)*

| | *n* | | OR[a] (95% CI) | *P* Value for Trend |
|---|---|---|---|---|
| | Cases | Controls | | |
| Vitamin E | | | | |
| Q1 (≤4.9 mg) | 128 | 354 | 1.00 | 0.002 |
| Q2 (5.0–6.8 mg) | 129 | 355 | 0.88 (0.64–1.22) | |
| Q3 (6.9–9.4 mg) | 135 | 362 | 0.82 (0.58–1.16) | |
| Q4 (>9.4 mg) | 104 | 354 | 0.58 (0.38–0.88) | |
| Retinol | | | | |
| Q1 (≤1,299 IU) | 139 | 362 | 1.00 | 0.81 |
| Q2 (1,300–2,117 IU) | 130 | 362 | 0.92 (0.67–1.25) | |
| Q3 (2,117–3,909 IU) | 120 | 354 | 0.84 (0.60–1.17) | |
| Q4 (>3,909 IU) | 107 | 347 | 0.71 (0.48–1.04) | |
| Vitamin A | | | | |
| Q1 (≤5,917 IU) | 135 | 353 | 1.00 | 0.04 |
| Q2 (5,918–9,225 IU) | 116 | 363 | 0.73 (0.53–1.01) | |
| Q3 (9,226–14,204 IU) | 131 | 361 | 0.82 (0.58–1.14) | |
| Q4 (>14,204 IU) | 114 | 348 | 0.66 (0.45–0.98) | |
| Total carotenoids | | | | |
| Q1 (≤3,808 IU) | 123 | 356 | 1.00 | 0.01 |
| Q2 (3,809–6,378 IU) | 125 | 356 | 0.86 (0.62–1.19) | |
| Q3 (6,379–10,311 IU) | 145 | 357 | 0.98 (0.71–1.36) | |
| Q4 (>10,311 IU) | 103 | 356 | 0.64 (0.43–0.93) | |
| α-Carotene | | | | |
| Q1 (≤445 μg) | 134 | 356 | 1.00 | 0.10 |
| Q2 (446–801 μg) | 130 | 357 | 0.95 (0.69–1.30) | |
| Q3 (802–1,576 μg) | 118 | 356 | 0.76 (0.55–1.06) | |
| Q4 (>1,576 μg) | 114 | 356 | 0.75 (0.53–1.06) | |
| β-Carotene | | | | |
| Q1 (≤3,043 μg) | 124 | 356 | 1.00 | 0.02 |
| Q2 (3,044–5,195 μg) | 129 | 357 | 0.90 (0.65–1.23) | |
| Q3 (5,196–8,349 μg) | 141 | 356 | 1.00 (0.72–1.39) | |
| Q4 (>8,349 μg) | 102 | 356 | 0.68 (0.46–0.98) | |
| Cryptoxanthin | | | | |
| Q1 (≤20 μg) | 126 | 356 | 1.00 | 0.97 |
| Q2 (21–81 μg) | 123 | 357 | 1.06 (0.77–1.45) | |
| Q3 (82–262 μg) | 116 | 356 | 0.95 (0.69–1.30) | |
| Q4 (>262 μg) | 131 | 356 | 1.11 (0.81–1.53) | |

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**Table 3.** *(Continued)*

| | *n* | | OR[a] (95% CI) | *P* Value for Trend |
|---|---|---|---|---|
| | Cases | Controls | | |
| Lutein + zeaxanthin | | | | |
| Q1 (≤2,748 μg) | 123 | 356 | 1.00 | 0.02 |
| Q2 (2,749–4,535 μg) | 104 | 357 | 0.87 (0.62–1.20) | |
| Q3 (4,536–7,101 μg) | 162 | 356 | 1.10 (0.80–1.51) | |
| Q4 (>7,101 μg) | 107 | 356 | 0.76 (0.52–1.10) | |
| Lycopene | | | | |
| Q1 (≤2,362 μg) | 119 | 356 | 1.00 | 0.16 |
| Q2 (2,363–4,319 μg) | 117 | 357 | 0.88 (0.64–1.21) | |
| Q3 (4,320–6,684 μg) | 145 | 356 | 1.02 (0.74–1.41) | |
| Q4 (>6,684 μg) | 115 | 356 | 0.81 (0.57–1.15) | |

*a:* Adjusted for age, education, region of residence, regularity of menstruation, family history of ovarian cancer, parity, age at menarche, oral contraceptive use, and total energy intake.

**Table 4.** ORs and 95% CIs for Risk of Ovarian Cancer With Monthly Frequency of Use of Selected Food Groups: Roswell Park Cancer Institute, Buffalo, NY (1982–96)

| | *n* | | OR[a] (95% CI) | *P* Value for Trend |
|---|---|---|---|---|
| | Cases | Controls | | |
| Fruits and fruit juices | | | | |
| Q1 (≤48) | 109 | 353 | 1.00 | 0.40 |
| Q2 (49–72) | 130 | 357 | 1.13 (0.81–1.56) | |
| Q3 (73–101) | 147 | 354 | 1.25 (0.90–1.74) | |
| Q4 (>101) | 110 | 361 | 0.85 (0.59–1.21) | |
| Vegetables | | | | |
| Q1 (≤24) | 106 | 351 | 1.00 | 0.07 |
| Q2 (25–42) | 134 | 364 | 1.06 (0.77–1.47) | |
| Q3 (43–66) | 155 | 355 | 1.21 (0.88–1.68) | |
| Q4 (>66) | 101 | 355 | 0.76 (0.52–1.10) | |
| Total fruits and vegetables | | | | |
| Q1 (≤80) | 107 | 347 | 1.00 | 0.09 |
| Q2 (81–117) | 137 | 362 | 1.11 (0.81–1.53) | |
| Q3 (118–164) | 162 | 364 | 1.17 (0.84–1.63) | |
| Q4 (>164) | 90 | 352 | 0.62 (0.42–0.92) | |
| Meats | | | | |
| Q1 (≤9) | 111 | 365 | 1.00 | 0.12 |
| Q2 (10–16) | 128 | 359 | 1.04 (0.76–1.44) | |
| Q3 (17–25) | 132 | 357 | 1.11 (0.80–1.54) | |
| Q4 (>25) | 125 | 344 | 1.17 (0.80–1.71) | |

*a:* Each food group adjusted for age, education, region of residence, regularity of menstruation, family history of ovarian cancer, parity, age at menarche, oral contraceptive use, and remaining food groups.



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ovarian cancer risk through effects on the endogenous hormonal milieu. Research has shown that levels of estriol, total estrogens, prolactin, and sex hormone-binding globulins can be affected through changes in fat, protein sources, and dietary fiber intakes (3–13).

There is a great deal of interest in the role of phytoestrogens in the etiology of hormone-sensitive cancers. It has been hypothesized that these compounds, available through dietary intake, could affect endogenous hormone metabolism through competitive inhibition of estrogen receptors or through substitution of less active estrogen metabolites (14). Although it was not possible to directly estimate because of the limited number of foods included in the FFQ, plant foods are good sources of phytoestrogens such as lignans. We observed significant reductions in risk associated with the highest intakes of dietary fiber. In a study of dietary phytochemical intake and breast cancer in Western New York, intakes of dietary fiber were highly correlated with intakes of lignans ($r = 0.84$; unpublished data). It is likely that the women in the present study also consume significant amounts of lignans, an exposure of potential importance in a hormone-sensitive disease such as ovarian cancer.

Several methodological issues should be considered in interpreting these results. As in all case-control studies, bias could have affected the validity of the findings. Selection bias may have occurred in this investigation. The ovarian cancer patient group was restricted to women who were treated at RPCI, a large regional cancer treatment center, and may not represent the general population of ovarian cancer patients in the Western New York region. However, it is unlikely that self-reported diet would be different for RPCI patients or women treated in different facilities. Furthermore, in this study, the control group consisted of female patients who received medical services at RPCI for a large variety of nonneoplastic conditions. The use of hospital controls might introduce bias because of the possibility that some controls were suffering from conditions that could affect dietary intake. However, it is unlikely that the hospital controls would be any more likely than the cases to alter their diet because of prevalent conditions. In addition, hospital controls were selected from a large pool of eligible participants with a wide variety of diagnostic groups, minimizing bias arising from potential overrepresentation of patients with characteristics that may be associated with exposure. Finally, as seen in Table 1, many previously identified risk factors for ovarian cancer were evident in our sample as well, suggesting that this source of bias was not substantial.

Selection bias may have also been introduced because of the low participation rate in this study. Only ~50% of eligible cases and controls agreed to complete the PEDS questionnaire. It is possible that women with more serious illness did not complete the questionnaire; these women may differ importantly from those who participated. We have no way to ascertain whether those women who refused to complete the instrument differed from participants with respect to the exposures of interest. Nonresponse is a serious problem in many epidemiological studies; our study obtained response rates similar to those commonly reported in the literature. Nevertheless, previous studies that utilized the PEDS database and faced the same methodological issue consistently replicated established epidemiological associations for a variety of cancer sites, including ovary (24–26), colon (27–30), breast (31,32), prostate (33,34), and lung (35,36).

There were marked differences between cases and controls with respect to place of residence, with ovarian cancer patients being more likely to live a greater distance from RPCI than controls. This is likely due to the fact that RPCI houses the Gilda Radner Familial Ovarian Cancer Registry, which acts as a referral center for patients with a suspected genetic predisposition for the development of ovarian cancer (37). However, other than residential history, observed epidemiological differences between cases and controls were consistent with those reported in the ovarian cancer literature (38–40).

Recall bias is always a problem in case-control studies of cancer. However, in this investigation, it may have been less of an issue because of our use of hospital controls. The questionnaire used in this investigation places no particular emphasis on any specific item. Thus there is little reason to believe that cases were more motivated than controls to recall diet. Exposure misclassification may also have affected our results, inasmuch as we based our analyses on self-reported diet and were not able to independently verify this information. Yet it is unlikely that this potential misclassification was differential in nature. In fact, our results confirm previous literature suggesting reduced risks of ovarian cancer associated with diets high in fruits and vegetables and associated nutrients (15–17,20–22).

Finally, the FFQ used to assess diet was limited, querying frequency of use of only 44 foods and beverages. Although these foods were selected to provide an adequate assessment of intakes of fruits and vegetables, dietary fiber, vitamins A and C, and the carotenoids, several important food groups and nutrients may have been neglected. The use of regression weights for nutrient calculation allows for estimation of nutrients not directly obtainable from the brief food list, but the relative validity of these estimates varies by nutrient. In a comparison of the 44-food questionnaire with two longer FFQs [the National Cancer Institute Health Habits and History ("Block") FFQ and the Harvard Semiquantitative FFQ], the brief FFQ provided estimates of dietary fiber, vitamins A and C, and carotenoids comparable to those obtained with the other two instruments (41). Estimates of total energy, fat, and fat components were less comparable (41). Notwithstanding these limitations, we nevertheless obtained estimates of risks for several nutrients that are consistent with previously reported studies (15–17,20–22).

It is unlikely that the lack of portion size information for the FFQ affected our results. In fact, the regression weights used to calculate nutrient intake are obtained from food frequency data that include portion size and frequency of use. This method is analogous to the use of a standard portion

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size in nutrient calculation. Furthermore, the availability of portion size information has not been shown to substantially improve nutrient intake estimates, inasmuch as subjects do not estimate portion size accurately and tend to ignore questions regarding portion size, and portion sizes vary less among individuals than do frequencies of use of specific foods (42–46).

A plant-based diet continues to be important in lowering risks of many cancers (1). Plant foods contain many substances, nutrient and nonnutrient, with potential to impact cancer development through effects on hormone metabolism, antioxidant activities, and other pathways (14). In conclusion, our results suggest that a diet high in fruits and vegetables and, consequently, dietary fiber, vitamin C, and carotenoids may play an important role in reducing the risk of ovarian cancer, independent of nondietary risk factors.

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## Acknowledgments and Notes

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