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## Dairy food, Calcium, and Risk of Cancer in the NIH-AARP Diet and Health Study

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### Abstract

**Background**—Dairy food and calcium have been hypothesized to play roles that differ among individual cancer sites, but the evidence has been limited and inconsistent. Moreover, the effect of dairy food and calcium on cancer in total is unclear.

**Methods**—Dairy food and calcium in relation to total cancer as well as cancer at individual sites were examined in the NIH-AARP Diet and Health Study. Intakes of dairy food and calcium from foods and supplements were assessed with a food frequency questionnaire. Incident cancer cases were identified through linkage with state cancer registries. Cox proportional hazard model was used to estimate relative risks (RRs) and tow-sided 95% confidence intervals (CI).

**Results**—During average of 7 years of follow-up, we identified 36,965 and 16,605 cancer cases in men and women, respectively. Calcium intake was not related to total cancer in men, but was nonlinearly associated with total cancer in women: risk decreased up to approximately 1,300 mg/day, above which no further risk reduction was observed. In both men and women, dairy food and calcium were inversely associated with cancers of the digestive system (multivariate RR for the highest quintile of total calcium vs. the lowest = 0.84, 95% CI: 0.77–0.92 in men and 0.77, 95% CI: 0.69–0.91 in women). Decreased risk was particularly pronounced with colorectal cancer. Supplemental calcium was also inversely associated with colorectal cancer risk.

**Conclusions**—Our study suggests that calcium intake is associated with lower risk of total cancer and cancers of the digestive system, especially colorectal cancer.

Because of the benefit of calcium on bone health  $^1$ , dietary guidance has emphasized intakes of both calcium and dairy food. For example, the Institute of Medicine recommends 1,200 mg/ day of calcium for adults 50 years old and over  $^1$  and the Dietary Guidelines for Americans, 2005 recommends 3 cups/day of fat-free or low-fat dairy food  $^2$ .

The role of dairy food and calcium in cancer, however, has engendered considerable controversy due to observations from epidemiologic studies of protective, null, and even positive associations for different organ sites  $^{3-7}$ . Dairy food and calcium have been consistently inversely associated with colorectal cancer <sup>3</sup>, whereas few studies have suggested

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possible inverse associations with lung and breast cancer <sup>4, 5</sup>. On the other hand, positive associations have been reported for prostate and ovarian cancer <sup>6, 7</sup>.

Because of limited evidence on the relation of dairy food and calcium to cancers at individual sites, especially cancers with a relatively low incidence, it has been difficult to assess the overall effect of dairy food and calcium on total cancer. Therefore, we examined in a large cohort of men and women whether intakes of dairy food and calcium were associated with risk of total cancer as well as cancer at multiple individual sites.

### METHODS

### Study population

The NIH-AARP Diet and Health Study, a collaboration between the National Institutes of Health (NIH) and AARP (formerly known as the American Association of Retired Persons), mailed a questionnaire to AARP members 50-71 years old and residing in one of six U.S. states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and two metropolitan areas (Atlanta, Georgia, and Detroit, Michigan) in 1995–96<sup>8</sup>. Among 567,169 participants who returned questionnaires, we excluded individuals who provided duplicate questionnaires (n=179), requested to be withdrawn (n=6), had moved out of the study area or died before baseline (n=582), indicated they were proxies for the intended respondents (n=15,760), had any prevalent cancer except non-melanoma skin cancer at baseline (n=51,193), and had reported end stage renal disease at baseline (n=997). In addition, we excluded individuals who reported extreme intakes (greater than twice the interquartile ranges above the 75<sup>th</sup> percentile or below the 25<sup>th</sup> percentile of sex-specific log transformed intake) of total energy (n=4,417) and calcium from foods (n=1,225). After these exclusions, the analytic cohort consisted of 293,907 men and 198,903 women. For analyses of ovarian and endometrial cancer, we excluded women who reported, respectively, a history of oophorectomy (n=43,536) and hysterectomy (n=81,025) at baseline. The study was approved by the National Cancer Institute (NCI) Special Studies Institutional Review Board.

### Dietary and risk factor assessment

At baseline in 1995–96, dietary intake was assessed with a self-administered 124 item food frequency questionnaire (FFQ), an earlier grid-based version of the Diet History Questionnaire developed at NCI<sup>9</sup>. Participants were asked to report their usual frequency of intake and portion size over the last 12 months, using 10 predefined frequency categories ranging from 'never' to '6+ times per day' for beverages, from 'never' to '2+ times per day' for solid foods, and 3 categories of portion size. The food items, portion sizes, and nutrient database were constructed using the U.S. Department of Agriculture (USDA)'s 1994–96 Continuing Survey of Food Intake by Individuals (CSFII) <sup>10, 11</sup>. The FFQ also inquired about frequency and types of multivitamins and frequency and dose of individual calcium supplements including Tums. Calcium intake was estimated from foods only (dietary calcium) and from foods and supplements combined (total calcium). Dietary calcium intake was adjusted for total energy intake using the residual method <sup>12</sup>.

Dairy food and its serving sizes was defined by the Pyramid Servings Database corresponding to the 1994–1996 CSFII, which utilizes a recipe file to disaggregate food mixtures into their component ingredients and assigns them to food groups. One serving of dairy food was defined according to standard portion sizes developed by USDA, such as 1 cup of milk or yogurt, 1.5 oz of natural cheese, or 2 oz of processed cheese <sup>13</sup>. We did not consider butter a dairy food because it has not generally been included in dairy food in previous studies and was not a major contributor to calcium intake.

The FFQ used in the study was calibrated against two non-consecutive 24-hour dietary recalls in 1,953 AARP participants <sup>14</sup>. The energy-adjusted correlation coefficient of dietary calcium intake between a FFQ and the reference method was 0.63 in men and 0.64 in women.

In the baseline questionnaire, we also asked about demographic characteristics, current body weight and height, medical history, family history of cancer, and lifestyle factors including frequency of vigorous physical activity that lasted at least 20 minutes, smoking status, time since quitting smoking, and smoking dose. In a subsequent questionnaire mailed in 1996–97, we inquired information on detailed medical history including medication use and prostate cancer screening using a prostate specific antigen (PSA) test.

### **Cancer ascertainment**

During follow-up from 1995 to 2003, cancer cases were identified through probabilistic linkage with cancer registry database from the original eight state and three additional states (Arizona, Nevada, and Texas). We have expanded cancer ascertainment areas to follow participants who moved to those states. The cancer registries are certified by the North American Association of Central Cancer Registries as being  $\geq$ 90% complete within two years of cancer occurrence. Our case ascertainment method has been described in a previous study, which demonstrated that approximately 90% of cancers were identified through the registries <sup>15</sup>. Vital status was ascertained through annual linkage of the cohort to the Social Security Administration Death Master File (SSADMF) in the U.S., follow-up searches of the National Death Index Plus for participants who matched to the SSADMF, cancer registry linkage, questionnaire responses, and responses to other mailings.

Incident cancer cases were invasive and comprised only the first malignancy diagnosed during the follow-up period if multiple cancers were diagnosed in the same participant. We defined cancers using the Surveillance Epidemiology and End Results (SEER) incidence site recode and the International Classification of Diseases for Oncology code ( $3^{rd}$  ed.): head and neck (C000-C009, C019-C119, C129-C140, C142-C148, C300-C301, C310-C329, C339-C349, C381-C384, C388, C390, C398, and C399), esophagus (C150-C159), stomach (C160-C169), colorectal (C180-C189, C199, C209, and C260), liver (C220 and C221), pancreas (C250-C259), lung (C340-C349), breast (C500-C509), ovarian (C569), endometrial (C540-C549, and C559), prostate (C619), bladder (C670-C679), kidney (C649 and C659), thyroid (C739), and brain (C710-C719) cancer. Non-Hodgkin lymphoma (NHL), leukemia, and myeloma were also defined by SEER definition. Total cancer included those cancers listed above, skin cancer excluding basal/squamous, other miscellaneous cancers, and unspecified cancers. We also grouped cancers by anatomical system; head and neck, digestive system, respiratory system (excluding larynx), reproductive system, urinary system, brain/other nervous system, endocrine system, and others. The definition of cancer in each anatomical system is provided in a footnote in figure 2.

### Statistical analysis

We estimated relative risks (RRs) and two-sided 95% confidence intervals (CI) with the Cox proportional hazards model <sup>16</sup> using the SAS PROC PHREG procedure <sup>17</sup>. We calculated person-years of follow-up time from the date of the baseline questionnaire until the date of a cancer diagnosis, death, move-out of the registry areas, or end of follow-up (Dec. 31, 2003), whichever occurred first. We confirmed that the proportional hazard assumption was met for the main exposures and covariates by including interaction terms with time and using the Wald chi-square procedure to test whether all coefficients equaled 0. For dairy food analyses, we used a nutrient density model, in which daily intake was expressed as number of pyramid servings per 1,000 kcal of total energy intake. The RRs were estimated according to sex-specific quintiles of dairy food and dietary and total calcium intakes. Supplemental calcium intake was

categorized into four groups, 0, >0 - <400, 400 - <1,000, and  $\geq 1,000$  mg/day. We performed a test for linear trend across quintiles/categories of intake by using the median value in each quintile/category.

In multivariate models, we adjusted for potential risk factors pertinent to individual cancers and listed covariates for site-specific cancers in footnotes in tables. Potential risk factors examined were race/ethnicity, education, marital status, body mass index (BMI), family history of cancer, vigorous physical activity, smoking status, time since quitting smoking, smoking dose, personal history of hypertension and diabetes, antacid use, consumption of alcohol and total beverages, intakes of fruits and vegetables, red meat, whole grains, tomatoes, total fat, protein, folate, alpha-linoleic acid, selenium and total energy, PSA test in men, and hormone replacement therapy use and its duration, parity, oral contraceptive use, age at menopause, and history of oophorectomy and hysterectomy in women. Dietary and supplemental calcium intakes were mutually adjusted in the multivariate models.

We assigned missing responses in most of covariates (missingness <4%) to their respective reference group after checking that cancer risk in individuals with such missing values did not statistically significantly differ from that of individuals in the reference group using a Wald-statistics. We, however, created an indicator variable for missing responses for smoking, antacid use, personal history of hypertension, and PSA test because individuals with missing response in those variables showed significantly different risk of cancer compared to their respective reference group. In sensitivity analyses, we analyzed the data using an indicator variable for missing responses in each covariate <sup>18, 19</sup> and also excluding participants with missing responses in any covariate <sup>20</sup> and found that the results from both methods were similar to those of the main analyses.

Whether the associations for dairy food and calcium intakes differed by sex were examined by including a cross-product term of sex and intake of dairy food or calcium and no significant interaction was observed.

We also tested whether dairy food and total calcium intakes were log-linearly associated with risk of total cancer by comparing a non-parametric regression curve obtained using restricted cubic splines with the linear model <sup>21</sup>. The likelihood ratio test and visual inspection of the restricted cubic splines were used. The number and location of the knots were identified through a stepwise selection process.

### RESULTS

During 3,383,377 person-years of follow-up, we identified 36,965 cancer cases in men and 16,605 cancer cases in women. The  $10^{\text{th}} - 90^{\text{th}}$  percentiles of dietary and total calcium and dairy food intake were 478–1,247 mg/day, 526–1,530 mg/day, and 0.3–2.9 servings/day, respectively, in men and 409–1,101 mg/day, 494–1,881 mg/day, and 0.3–2.7 servings/day, respectively, in women. Dairy food was positively correlated with dietary calcium (r = 0.83 in men and 0.82 in women) and total calcium (r = 0.68 in men and 0.47 in women), and dietary calcium was also positively correlated with total calcium (r =0.83 in men and 0.60 in women). The prevalence of calcium containing multivitamin use was 49% in men and 57% in women, and the prevalence of individual calcium supplement use (≥4 times/week) was 14% in men and 41% in women.

Compared to participants in the lowest quintile of dairy food or total calcium intake, participants in the highest quintile were more likely to be non-Hispanic White, to be college educated, to be physically active, and to be current hormone replacement therapy users among women, but they were less likely to smoke cigarettes and to drink alcohol (Table 1). Women in the highest quintile of total calcium intake had a lower BMI than those in the lowest quintile.

Total calcium intake was not associated with risk of total cancer incidence in men, but it was non-linearly associated with the risk of total cancer incidence in women (p for non-linearity = 0.05, Figure 1). In non-parametric regression analyses, the RRs for total cancer incidence in women decreased up to approximately 1,300 mg/day of total calcium intake and no further risk reduction was observed above 1,300 mg/day. The association between total calcium intake and risk of total cancer did not differ by cancer stages or cancer grades (data not shown). In a secondary analysis excluding non-aggressive prostate cancer that contributed to a large proportion of total cancer cases, we observed a weak inverse association between total calcium and total cancer incidence in men. With the lowest quintile of total calcium intake as reference, the multivariate RRs for total cancer incidence in the second through the highest quintile were 1.00, 0.98, 0.99, and 0.96 (95% CI: 0.92–1.02, p trend=0.16) in men.

Dairy food and dietary and supplemental calcium were not related to total cancer incidence in men, whereas dietary calcium, but not dairy food or supplemental calcium, was inversely related to total cancer incidence in women (Table 2 and 3). When cancers diagnosed during the first 2 years of follow-up were excluded, the association with total cancer became slightly stronger for dietary calcium in men (multivariate RR in the highest quintile vs. the lowest (RR<sub>Q5 vs. Q1</sub>) = 0.96, 95% CI: 0.92–1.00, p trend=0.05, n=27,720 cases) and for dairy food in women (multivariate RR<sub>O5 vs. Q1</sub> = 0.93, 95% CI: 0.88–0.99, p trend=0.01, n=12,395 cases).

Death from total cancer and death from cardiovascular disease (CVD) in relation to dairy food and calcium intakes were examined. Dairy food and dietary, supplemental and total calcium intakes were not associated with total cancer mortality in both men (n=8,787 death) and women (n=4,479 death): the multivariate RR<sub>Q5 vs. Q1</sub> for dairy food and total calcium were 1.05 (95% CI: 0.97–1.14) and 1.02 (95% CI: 0.94–1.11), respectively, in men and 0.93 (95% CI: 0.84–1.04) and 0.97 (95% CI:0.87–1.08), respectively, in women.

Total calcium intake was related to a 16% lower risk of cancers of the digestive system in men (multivariate  $RR_{Q5 \text{ vs. }Q1} = 0.84, 95\%$  CI: 0.77–0.92) and a 23% lower risk in women (multivariate  $RR_{Q5 \text{ vs. }Q1} = 0.77, 95\%$  CI: 0.69–0.91, Figure 2). Similar inverse association with cancers of the digestive system was observed for dairy food intake in both men and women (data not shown). Total calcium and dairy food intakes were not associated with cancer in any other anatomical systems.

For specific cancers in men, dairy food was inversely associated with cancers of head and neck, esophagus, stomach, colorectum, and bladder, whereas it was positively associated with prostate cancer (Table 2). Dietary and supplemental calcium were also significantly inversely associated with colorectal cancer. Total calcium was significantly related to a lower risk of colorectal cancer and showed a weak inverse association with kidney cancer. On the other hand, total calcium was not related to prostate cancer.

In women, dairy food was significantly inversely associated with colorectal cancer and showed a weak inverse association with stomach cancer (Table 3). Dietary, supplemental, and total calcium were also inversely related to colorectal cancer. Supplemental calcium was also inversely associated with liver cancer, while total calcium was related to an increased risk of NHL. Dairy food, dietary, supplemental, and total calcium were not related to breast, ovarian, and endometrial cancer.

When we examined the associations among men and women combined, we found that the results for esophageal, stomach, liver, pancreatic, and brain cancer were similar to those for men alone. We also observed that total calcium was now significantly inversely associated with kidney cancer (the multivariate  $RR_{O5 \text{ ys},O1} = 0.77, 95\%$  CI: 0.63–0.94, p trend=0.01).

### DISCUSSION

In this large prospective cohort study, we found that total calcium was nonlinearly associated with total cancer incidence in women: risk decreased up to approximately 1,300 mg/day, after which no further risk reduction was observed. The associations with dairy food and calcium differed among individual cancer sites. Dairy food and calcium were inversely associated with cancers of the digestive system in both men and women, especially with colorectal cancer. Supplemental calcium was also inversely associated with colorectal cancer. Calcium intake was not related to breast or prostate cancer.

Dairy food and calcium have been hypothesized to play roles that differ among individual cancer sites. Dairy food, relatively high in potentially anticarcinogenic nutrients such as calcium, vitamin D, and conjugated linoleic acid have been postulated to protect against the development of colorectal and breast cancer <sup>4</sup>, <sup>22</sup>. Calcium has been shown to reduce proliferation, stimulate differentiation, and induce apoptosis in cells in gastrointestinal tract and breast <sup>23</sup>, <sup>24</sup>. In addition, the binding of calcium to bile and fatty acids in gastrointestinal tract has been hypothesized to reduce damage to large bowel mucosa <sup>23</sup>. Nevertheless, high calcium intake has been hypothesized to increase the risk of prostate cancer by suppressing 1,25(OH)<sub>2</sub> vitamin D and thereby offsetting a potential anti-carcinogenic effect of vitamin D <sup>25</sup>. Dairy food has also been found to increase insulin-like growth factor (IGF)-I, a potent mitogen associated with increased risk of prostate cancer <sup>26</sup>, <sup>27</sup>.

We found that total calcium was non-linearly inversely associated with total cancer in women. In contrast, the Women's Health Initiative Study, a randomized clinical trial of daily supplementation of 1,000 mg calcium combined with 400 IU vitamin D for an average of seven years, found no effect on total cancer incidence among postmenopausal women (Hazard ratio = 0.98, 95% CI: 0.91–1.05, total cancer cases = 1,634 in treatment group and 1,655 in placebo group)<sup>28</sup>. We note, however, that in the WHI study, two third of women had at least 800 mg/ day of the total calcium at baseline and total number of cancer cases were small.

Consistent with previous studies <sup>3</sup>, <sup>22</sup>, we found that intakes of dairy food and calcium were significantly inversely associated with risk of colorectal cancer. In a pooled analysis of 10 cohort studies <sup>3</sup>, a 15–20% lower risk of colorectal cancer was observed for total calcium (relative risk (RR)= 0.78, 95% CI: 0.69–0.88 for the highest vs. lowest quintile) and milk (RR=0.85, 95% CI: 0.78–0.94 for <70 vs.  $\geq$ 250 g/day). In addition, randomized clinical trials have found that calcium supplementation reduced recurrence of colorectal adenomas, precursors of colorectal cancer <sup>29</sup>, <sup>30</sup>.

A limited number of studies, most with case-control designs, have examined dairy food and calcium in relation to head and neck, esophageal, and stomach cancer. Few studies have observed inverse associations of dairy food and calcium with head and neck <sup>31, 32</sup> and esophageal cancer <sup>33–35</sup>; other studies have found no associations with cancer in head and neck <sup>36</sup>, esophagus <sup>37–41</sup>, and stomach <sup>33, 34, 41, 42</sup>. Our study is one of the first large prospective cohort studies examining dairy food and calcium in relation to these cancers. We found that dairy food and dietary calcium were inversely associated with cancers of the digestive system in men, while supplemental and total calcium showed suggestive inverse associations in women. Calcium supplement use in men tended to be less prevalent and consistent, and therefore more likely to be measured with error; this may explain why the calcium associations for supplemental and total calcium intakes did not achieve statistical significances, but the numbers of cases for these cancers were small. Overall, these findings suggest that calcium plays a role in preventing cancers of the digestive system. However, we cannot exclude the possibility of confounding by vitamin D found in dairy food and supplements. Vitamin D, tightly related to

calcium regulation in the body, has been inversely associated with digestive system cancers in other studies<sup>43</sup>.

In women, supplemental calcium was inversely associated with liver cancer, but it was positively related to NHL. Given that the association with liver cancer was observed in women only that the number of liver cancer cases was small, this finding is likely due to chance. Few studies <sup>44–47</sup> which investigated the association between dairy food or calcium and NHL suggested that dairy food was associated with an increased risk of NHL. Further investigation of dairy food and calcium in relation to cancers in liver and NHL is warranted.

The associations between dairy food and calcium and breast cancer have been either null or inverse  $^{4, 48-51}$ . Cohort studies which found dairy food and calcium to be inversely associated with breast cancer suggested that the associations may differ by menopausal status  $^{49, 50}$  or estrogen receptor status of the tumor  $^{51}$ . Our study, conducted mainly among postmenopausal women, found that dairy food and calcium were not associated with breast cancer. Further studies examining the associations by tumor characteristics of breast cancer and by menopausal status might be informative.

Despite the existence of plausible biologic mechanisms, the effects of dairy food and calcium on prostate cancer are unclear. Epidemiologic studies have found null <sup>52–54</sup> as well as positive <sup>7, 55–57</sup> associations for dairy food and calcium. Among studies that observed a positive association between calcium and prostate cancer, a significantly increased risk was generally found only with very high calcium intake (2000 mg/day, compared with approximately <750 mg/day) or in advanced prostate cancer <sup>7, 55</sup>. However, our study found that calcium, even at very high intake of calcium ( $\geq$ 2000 vs. 500–<750 mg/day), was not associated with prostate cancer <sup>58</sup>.

Some limitations exist in our study. First, we did not examine if associations with dairy food and calcium differed by tumor subtype or tumor aggressiveness of site-specific cancers. It is possible that we missed some associations that may exist only for certain tumor subtypes or aggressive tumors. Second, although we adjusted for all potential risk factors available in our study for site-specific cancers, residual confounding by unknown or unmeasured risk factors may exist for some cancers. Third, in analyses of low incidence cancers, especially cancers in women with small numbers of cases, we had limited statistical power to examine an association and some findings may be due to chance. Lastly, because diet was assessed only once at baseline, this may not reflect long-term usual intake as accurately as repeated measurements of diet during follow-up. Also, we could not examine if dairy food and calcium intakes during earlier life periods or lifelong cumulative intakes are related to cancer risk.

Nevertheless, our study is one of the first cohort studies to examine dairy food and calcium in relation to total cancer as well as low incidence cancers. Moreover, our prospective design avoids the recall and selection biases that can affect results from case-control studies. Our study had high statistical power with more than 53,000 total cancers and at least 100 cases for most individual cancers. Thus substantial effects of dairy food and calcium were unlikely to have been missed. A further strength of our study is that we rigorously controlled for all potential risk factors including both dietary and lifestyle factors for each site-specific cancer.

In conclusion, our findings suggest that calcium intake consistent with current recommendations is associated with a lower risk of total cancer in women and cancers of the digestive system, especially colorectal cancer in both men and women.

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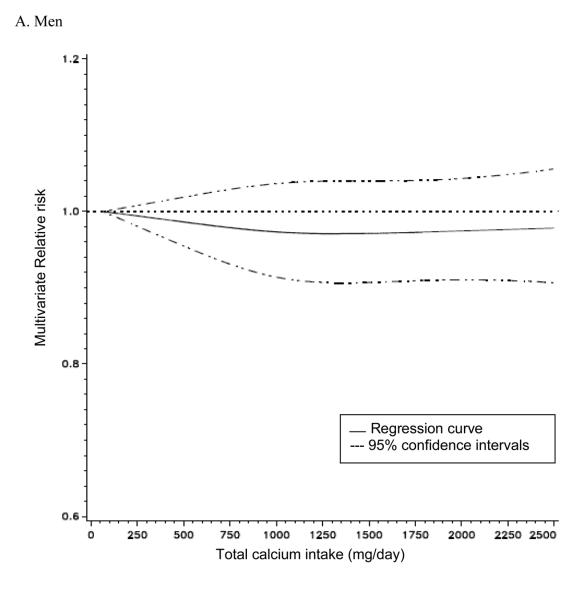
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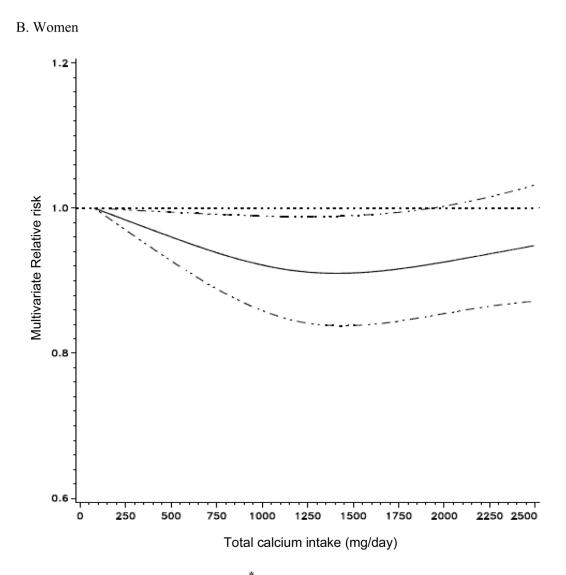
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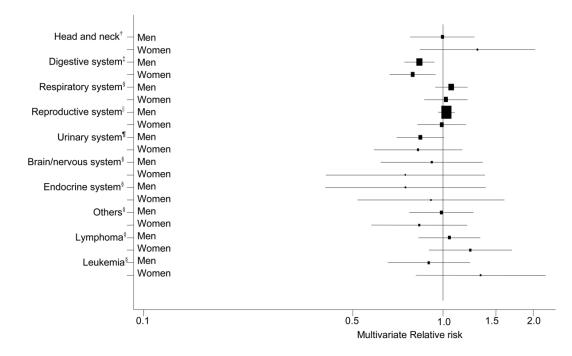
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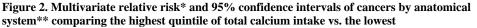




## Figure 1. Non-parametric regression curve<sup>\*</sup> for the association between total calcium intake and risk of all cancers

\* A Men: the model adjusted for race/ethnicity, education, marital status, body mass index, family history of cancer, vigorous physical activity, smoking status, time since quitting smoking, smoking dose, antacid use, personal history of diabetes and hypertension, PSA test, alcohol, and intakes of fat, red meat, fruit and vegetables, whole grains, protein, beverages, folate, tomatoes, alpha-linolenic acid, selenium and total energy. B. Women: the model adjusted for race/ethnicity, education, marital status, body mass index, family history of cancer, vigorous physical activity, smoking status, time since quitting smoking, smoking dose, antacid use, age at menopause, parity, oral contraceptive use, HRT use, duration of hormone replacement therapy use, personal history of diabetes, hypertension, oophorectomy and hysterectomy, alcohol, and intakes of fat, red meat, fruit and vegetables, whole grains, total beverages, protein, folate and total energy.





\* Adjusted for race/ethnicity, education, marital status, BMI, family history of cancer, vigorous physical activity, alcohol and intakes of red meat and total energy + additional variables listed in each footnote. The squares and horizontal lines correspond with the multivariate RR and 95% CI.

<sup>†</sup> Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, intake of fruit and vegetables, and menopausal hormone therapy (MHT) use in women.

‡ Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, MHT use in women, antacid use, intakes of fruit and vegetables, whole grains, and folate

§ Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, and MHT use in women.

|| Adjusted for variables listed in the asterisked footnote + smoking, personal history of diabetes, PSA test, and intakes of tomatoes, alpha-linolenic acid, and selenium in men. For women, the model was adjusted for variables listed in the asterisked footnote + smoking, MHT use, parity, oral contraceptive use, personal history of oophorectomy and hysterectomy, and intake of fat. ¶ Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, personal history of diabetes and hypertension, parity, MHT and oral contraceptive use in women, and intakes of fruit and vegetables, total beverages, and protein. \*\* Cancers in each anatomical system are: digestive system (C150-C189, C199, C209-C212, C218, C220-C221, C239-C260, C268-C269, C480-C482, C488), respiratory system excluding larynx (C300-C301, C310-C319, C339-C349, C381-C384, C388, C390, C398, C399), reproductive system (men: C600-C609, C619-C639; women: C510-C519, C529-C549, C559, C569-C589), urinary system (C649, C659, C669-C689), brain/other nervous system (C700-C729), and endocrine system (C739-C759, C379).

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Table 1

Selected characteristics of study participants by categories of dairy food and total calcium intakes

		Dally rough						
	M	Men	Wo	Women	M	Men	Woi	Women
	Quintile 1	Quintile 5	Quintile 1	Quintile 5	Quintile 1	Quintile 5	Quintile 1	Quintile 5
Dairy food $^{\dagger}$ (serving/1,000 kcal)	0.2	1.4	0.2	1.6	0.3	1.4	0.3	1.2
Dietary calcium $^{\dagger}$ (mg/day)	496	1325	428	1157	491	1239	451	925
Supplemental calcium <sup><math>\dagger</math></sup> (mg/day)	141	149	356	388	20	398	29	1037
White, non-Hispanic (%)	87	94	82	93	06	94	84	94
College and postcollege (%)	40	45	27	32	39	48	23	37
Married (%)	83	84	45	41	84	84	45	45
Body mass index $({ m kg/m^2})^{\dagger}$	27.1	27.3	26.8	26.7	27.3	27.1	27.5	25.8
Family history of any cancer (%)	46	47	50	51	47	47	50	52
Current smokers (%)	13	10	19	12	15	8	21	6
>20 cigarettes/day among ever smokers (%)	50	47	31	28	50	48	32	31
Quit smoking ≥10 years ago among former smokers (%)	70	72	57	63	69	73	55	99
Physical activity, ≥5 times/week (%)	21	22	15	18	17	25	11	22
Personal history of diabetes (%)	8	13	7	6	7	12	7	5
Personal history of hypertension (%)	42	40	41	40	39	36	41	33
Antacid use (%)	22	33	19	27	30	32	25	34
Current menopausal hormone therapy use (%)	ı	ı	41	45	ı	ı	35	54
Multivitamin use (%)	49	54	54	64	26	71	30	62
Alcohol (g/day) <sup>†</sup>	31	6	6	4	32	10	6	5
Fruit and vegetables (servings/1,000 kcal) $^{\dagger}$	3.7	3.4	4.7	4.1	3.1	3.8	3.9	4.8
Red meat $(g/1,000 \text{ kcal})^{\dagger}$	41	32	32	24	45	30	37	23
Whole grains (servings/1,000 kcal) $^{\ddagger}$	0.6	0.7	0.6	0.7	0.5	0.8	0.6	0.7
Total fat (% of energy) <sup><math>\dagger</math></sup>	30	29	31	27	31	28	33	27
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		Dairy	Dairy foods			Total calcium*	alcium*	
	W	Men	Wo	Women	Μ	Men	Women	nen
	Quintile	Quintile	Quintile	Quintile	Quintile	Quintile	Quintile	Quintile
	1	w	1	Ŋ	1	S	1	ŝ
Total energy $(kcal/day)^{\dagger}$	2065	1959	1542	1545	2044	2035	1594	1538
* Calcium from diet and supplements combined $\stackrel{*}{\uparrow}$ Mean value								

IAll cancers* (n=36,965%)Dairy foodsDairy foodsDietary calciumSupplemental calcium1.00Yotal calcium1.00Head and neck cancer// (n=1,038)Dairy foodsDietary calcium1.00Dietary calcium1.00Supplemental calciumDietary calcium1.00Dietary calcium1.00Pietary foodsDietary calcium1.00Dairy foodsDietary calcium1.00Dietary calcium1.00Supplemental calcium1.00Dietary calcium1.00Dietary calcium1.00Dietary calcium1.00Dietary calcium1.00			Categories <sup>†</sup>			
n=1,038) 68)		2	3	4	S	- p trend
_		1.02 (0.98–1.05)	1.02 (0.99–1.06)	1.04(1.01-1.08)	1.03 (0.99–1.07)	0.19
_		1.00 (0.96–1.03)	0.99(0.96 - 1.03)	$1.01 \ (0.97 - 1.05)$	1.00 (0.96–1.05)	0.76
		0.97 (0.94–1.00)	0.97 (0.93–1.01)	0.96(0.90 - 1.03)		0.18
_		0.99 (0.96–1.03)	0.99 (0.96–1.03)	0.95(0.96 - 1.03)	0.99 (0.95–1.03)	0.74
		0.98 (0.82–1.18)	$0.89\ (0.74{-}1.08)$	0.87 (0.72–1.06)	$0.84\ (0.69{-}1.02)$	0.05
_		0.93 (0.78–1.12)	0.84 (0.69–1.02)	0.92 (0.76–1.12)	0.78 (0.64–0.96)	0.03
		1.21 (1.06–1.38)	1.22 (0.98–1.52)	1.18 (0.81–1.73)		0.07
_		1.00(0.83 - 1.20)	0.90(0.74 - 1.10)	0.99 (0.82–1.21)	0.99 (0.81–1.21)	0.99
		1.11 (0.85–1.46)	1.07 (0.82–1.41)	0.75 (0.55–1.02)	0.70 (0.51–0.96)	0.002
		0.91 (0.70–1.19)	0.72 (0.54–0.97)	$0.75\ (0.56{-}1.00)$	$0.66\ (0.49-0.90)$	0.01
	-	$0.94\ (0.77 - 1.15)$	1.21 (0.89–1.63)	1.32 (0.80–2.17)	ı	0.14
Total calcium 1.00	-	0.98 (0.74–1.29)	0.84 (0.63–1.13)	$0.89\ (0.67 - 1.19)$	0.84 (0.62–1.13)	0.23
Stomach cancer <sup>**</sup> (n=512)						
Dairy foods 1.00		1.03(0.80 - 1.34)	0.95 (0.73–1.24)	0.72~(0.54-0.96)	0.80 (0.61–1.06)	0.03
Dietary calcium 1.00		1.13(0.87 - 1.47)	0.95 (0.72–1.25)	0.93 (0.70–1.24)	0.87 (0.65–1.16)	0.15
Supplemental calcium 1.00		1.12 (0.92–1.35)	0.99 (0.72–1.36)	1.51 (0.95–2.39)		0.17
Total calcium 1.00		1.07(0.81 - 1.41)	1.13 (0.86–1.48)	1.04 (0.79–1.38)	0.96 (0.72–1.29)	0.58
Colorectal cancer $\dagger^{\dagger}$ (n=3,463)						
Dairy foods 1.00	-	$0.91\ (0.82{-}1.01)$	0.83 (0.75–0.93)	(0.80-0.90)	0.85 (0.76–0.94)	0.01
Dietary calcium 1.00		0.86(0.77 - 0.95)	0.83 (0.74–0.92)	0.85 (0.76–0.95)	0.84 (0.75–0.94)	0.03
Supplemental calcium 1.00	-	0.96(0.88 - 1.05)	0.91(0.79 - 1.04)	0.74 (0.58–0.94)		0.01
Total calcium 1.00		0.89 (0.80–0.98)	0.83 (0.75–0.93)	0.87 (0.78–0.97)	0.79 (0.70–0.89)	0.001
Liver cancer <sup><math>\ddagger \ddagger</math> (n=311)</sup>						
Dairy foods 1.00		1.02 (0.72–1.45)	1.05 (0.74–1.50)	1.07 (0.75–1.52)	1.04 (0.72–1.48)	0.84

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Table 2

			${f Categories}^{\dagger}$			
	1	2	3	4	S	b riena
Dietary calcium	1.00	0.84 (0.59–1.19)	0.97 (0.69–1.38)	0.87 (0.61–1.26)	0.99 (0.69–1.42)	0.86
Supplemental calcium	1.00	0.92 (0.72–1.17)	0.78 (0.50–1.20)	1.03 (0.53–2.03)		0.54
Total calcium	1.00	$0.75\ (0.52{-}1.08)$	1.20 (0.87–1.67)	$0.83\ (0.58-1.20)$	0.88 (0.61–1.27)	0.61
Pancreatic cancer <sup>§§</sup> (n=717)						
Dairy foods	1.00	0.96 (0.76–1.20)	1.01 (0.80–1.27)	1.00 (0.79–1.26)	$0.82\ (0.64{-}1.05)$	0.13
Dietary calcium	1.00	0.94 (0.75–1.18)	1.04 (0.83–1.31)	0.92 (0.72–1.16)	$0.82\ (0.64{-}1.06)$	0.11
Supplemental calcium	1.00	0.95(0.81 - 1.11)	0.90 (0.69–1.19)	1.17 (0.77–1.77)		06.0
Total calcium	1.00	0.93(0.74 - 1.16)	0.90 (0.72–1.14)	0.98 (0.78–1.23)	0.87 (0.68–1.11)	0.39
Lung cancer <sup>§§</sup> (n=4,287)						
Dairy foods	1.00	1.04(0.94 - 1.14)	1.01 (0.92–1.11)	1.04 (0.95–1.15)	1.05(0.95 - 1.16)	0.36
Dietary calcium	1.00	$0.97\ (0.89-1.07)$	1.02 (0.93–1.13)	1.04 (0.95–1.15)	1.00(0.91 - 1.11)	0.68
Supplemental calcium	1.00	0.97 (0.91 - 1.03)	1.03 (0.92–1.15)	1.04 (0.86–1.27)		0.64
Total calcium	1.00	1.05(0.96 - 1.15)	1.03 (0.94–1.13)	1.03 (0.94–1.13)	1.03(0.93 - 1.13)	0.76
Prostate cancer <sup>     </sup> (n=17,189)						
Dairy foods	1.00	1.02(0.97 - 1.07)	1.05 (1.00–1.10)	1.06 (1.01–1.12)	1.06 (1.01–1.12)	0.01
Dietary calcium	1.00	1.01 (0.96–1.06)	1.00 (0.95–1.05)	1.03 (0.98–1.08)	1.04(0.98-1.09)	0.14
Supplemental calcium	1.00	0.99 (0.95–1.02)	0.97 (0.92–1.03)	0.96 (0.88–1.05)		0.21
Total calcium	1.00	0.99(0.95 - 1.04)	1.01 (0.96–1.06)	1.00(0.95 - 1.05)	1.03(0.98 - 1.08)	0.21
Bladder cancer <sup>¶¶</sup> (n=1,417)						
Dairy foods	1.00	1.02 (0.86–1.19)	$0.94\ (0.80-1.11)$	0.85 (0.72–1.01)	0.86 (0.72–1.02)	0.03
Dietary calcium	1.00	1.14(0.97 - 1.34)	0.99 (0.84–1.17)	0.90 (0.75–1.07)	0.94 (0.78–1.12)	0.10
Supplemental calcium	1.00	0.90(0.80 - 1.01)	0.99 (0.83–1.20)	$0.84\ (0.59-1.18)$		0.34
Total calcium	1.00	0.96(0.82 - 1.13)	0.82 (0.69–0.97)	0.87 (0.73–1.03)	0.87 (0.73–1.03)	0.11
Kidney cancer <sup>***</sup> (n=991)						
Dairy foods	1.00	1.06(0.86 - 1.30)	1.09 (0.89–1.34)	1.12(0.91-1.38)	$1.08\ (0.87 - 1.35)$	0.54
Dietary calcium	1.00	0.93 (0.76–1.14)	0.93 (0.75–1.14)	0.97 (0.78–1.20)	0.98 (0.78–1.24)	0.86
Supplemental calcium	1.00	0.89 (0.77–1.02)	0.86 (0.68–1.09)	0.90 (0.61–1.34)	ı	0.22
Total calcium	1.00	0.90(0.74 - 1.10)	0.93 (0.76–1.14)	0.94 (0.76–1.15)	0.80(0.64 - 1.01)	0.10
Thyroid cancer <sup>‡‡</sup> (n=170)						
Dairy foods	1.00	1.02 (0.60–1.72)	1.48 (0.91–2.42)	1.59 (0.98–2.57)	0.78 (0.45–1.37)	0.41

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	1	2	3	4	S	
Dietary calcium	1.00	1.53 (0.90–2.62)	1.67 (0.98–2.84)	1.71 (1.00–2.91)	1.19 (0.67–2.12)	86.0
Supplemental calcium	1.00	0.85 (0.61–1.17)	0.92 (0.54–1.57)	0.70 (0.26–1.91)		0.44
Total calcium	1.00	0.95 (0.58–1.56)	1.07 (0.66–1.74)	1.15 (0.71–1.87)	0.79 (0.46–1.34)	0.43
Brain cancer <sup>‡‡</sup> (n=390)						
Dairy foods	1.00	0.82(0.59 - 1.14)	0.89 (0.64–1.22)	1.01 (0.74–1.37)	0.83 (0.60–1.14)	0.52
Dietary calcium	1.00	0.81 (0.58–1.13)	1.02 (0.74–1.39)	0.77 (0.55–1.08)	0.91 (0.65–1.26)	0.65
Supplemental calcium	1.00	1.18 (0.95–1.46)	1.31(0.94 - 1.83)	1.11 (0.62–1.99)		0.25
Total calcium	1.00	0.79~(0.57 - 1.10)	0.82 (0.59–1.13)	0.91 (0.66–1.25)	0.89 (0.65–1.23)	0.98
Non-Hodgkin Lymphoma <sup>‡‡</sup> (n=1,267)	n=1,267)					
Dairy foods	1.00	0.92 (0.76–1.10)	1.09(0.91 - 1.30)	1.06 (0.89–1.27)	1.02 (0.85–1.22)	0.56
Dietary calcium	1.00	0.97 (0.81–1.17)	1.01(0.84 - 1.21)	1.11 (0.93–1.33)	1.00(0.83 - 1.20)	0.76
Supplemental calcium	1.00	0.84 (0.74–0.95)	0.87 (0.71–1.07)	0.99 (0.72–1.36)		0.33
Total calcium	1.00	1.03 (0.86–1.24)	1.15 (0.96–1.38)	0.95(0.79 - 1.14)	1.02 (0.85–1.23)	0.77
Leukemia‡‡ (n=757)						
Dairy foods	1.00	1.16 (0.92–1.46)	0.93 (0.73–1.19)	1.16(0.92 - 1.47)	1.11 (0.88–1.41)	0.41
Dietary calcium	1.00	0.90 (0.72–1.13)	0.82(0.65 - 1.04)	0.95 (0.76–1.19)	0.87 (0.69–1.11)	0.49
Supplemental calcium	1.00	1.17 (1.01–1.36)	0.96 (0.73–1.25)	0.93 (0.59–1.47)	·	0.78
Total calcium	1.00	0.93 (0.74–1.17)	0.95 (0.75–1.19)	0.96 (0.76–1.21)	0.88 (0.69–1.21)	0.38
Myeloma <sup>‡‡</sup> (n=369)						
Dairy foods	1.00	1.06 (0.75–1.49)	1.38 (1.00–1.92)	1.15(0.81 - 1.61)	1.14(0.81 - 1.61)	0.63
Dietary calcium	1.00	1.08 (0.77–1.51)	1.07 (0.76–1.50)	1.27 (0.91–1.77)	1.05 (0.74–1.50)	0.71
Supplemental calcium	1.00	0.92 (0.74–1.14)	0.69(0.46 - 1.04)	0.60 (0.28–1.27)		0.04
Total calcium	1.00	1.03(0.74 - 1.43)	1.07 (0.77–1.48)	$0.91 \ (0.65 - 1.28)$	0.92(0.65 - 1.30)	0.42

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478, 616, 739, 899 and 1247 mg/day for dietary calcium; and 526, 498, 857, 1073, and 1530 mg/day for total calcium. Supplemental calcium intake was categorized into four groups, 0, >0-<400, 400-<1,000, and ≥1,000 mg/day. Dietary and supplemental calcium intakes were mutually adjusted in the multivariate models.

<5.5-<15, 15-<30, and 230 g/day), and intakes of red meat (quintiles) and total energy (continuous) and additional variables listed in each footnote below.</p>

<sup>4</sup> Adjusted for variables listed in the asterisked footnote + smoking status (never, former, and current), time since quitting smoking (never, stopped >10 years ago, stopped 5–9 years ago, stopped 1–4 years ago, stopped <1 year ago, and currently smoking), smoking dose (0, 1–10, 11–20, 21–30, 31–40, 41–50, 51–60, >60 cigarettes/day), antacid use (yes, no), personal history of diabetes (yes, no) and hypertension (yes, no), PSA test (yes, no), and intakes of fat (quintiles), fruit and vegetables (quintiles), whole grains (quintiles), protein (quintiles), total beverages (quintiles), folate (quintiles), tomatoes (quintiles), alphalinolenic acid (quintiles), and selenium (quintiles).

 $^{S}$ Number of cases

// Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, and intakes of fruit and vegetables.

Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, antacid use, and intake of fruit and vegetables.

Adjusted for variables listed in the asterisked footnote + smoking (never, <20 cigarettes/day in the past, >20 cigarettes/day in the past, currently <20 cigarettes/day, and currently >20 cigarettes/day), and antacid use. \*\*

 $\dot{r}^{\dagger}$  Adjusted for variables listed in the asterisked footnote + smoking, and intakes of fruit and vegetables, whole grains, and folate.

 $\overset{++}{}^{+}$  Adjusted for variables listed in the asterisked footnote + smoking.

\$ djusted for variables listed in the asterisked footnote +smoking status, time since quitting smoking, and smoking dose.

//// Adjusted for variables listed in the asterisked footnote + smoking, personal history of diabetes, PSA test, and intakes of tomatoes, alpha-linolenic acid, and selenium.

Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, and intakes of fruit and vegetables, and total beverages.

Adjusted for variables listed in the asterisked footnote + smoking, personal history of diabetes and hypertension, and intake of protein. \*\*\*

I			$Categories^T$			
	1	2	3	4	w	p trend
All cancers <sup><math>\ddagger</math></sup> (n=16,605 <sup>§</sup> )						
Dairy foods	1.00	0.98 (0.94–1.03)	0.95(0.90-1.00)	0.97 (0.92–1.02)	0.95(0.90-1.00)	0.10
Dietary calcium	1.00	0.96(0.91 - 1.00)	0.95(0.90-1.00)	0.95(0.90-1.01)	0.93(0.87 - 0.99)	0.04
Supplemental calcium	1.00	0.97 (0.92–1.01)	0.95(0.91 - 1.00)	0.96 (0.91–1.02)		0.28
Total calcium	1.00	0.98 (0.93–1.03)	0.94 (0.89 - 0.99)	0.93 (0.88 - 0.98)	0.96 (0.91–1.02)	0.23
Head and neck cancer// (n=325)	()					
Dairy foods	1.00	0.75 (0.53–1.05)	0.90 (0.64–1.25)	1.02 (0.73–1.41)	0.89 (0.63–1.27)	0.99
Dietary calcium	1.00	0.92 (0.66–1.28)	1.09(0.79 - 1.52)	$0.98\ (0.69-1.40)$	1.03 (0.72–1.47)	0.80
Supplemental calcium	1.00	1.16(0.88 - 1.52)	1.22 (0.90–1.66)	1.05 (0.72–1.53)		0.75
Total calcium	1.00	1.33(0.97 - 1.83)	$0.92\ (0.64 - 1.31)$	1.02 (0.71–1.46)	1.30 (0.91–1.86)	0.42
Esophageal cancer¶ (n=79)						
Dairy foods	1.00	$0.82\ (0.42 - 1.60)$	1.21 (0.65–2.25)	0.85 (0.42–1.72)	0.64 (0.29–1.44)	0.31
Dietary calcium	1.00	0.83 (0.44–1.57)	1.03(0.55 - 1.94)	0.68 (0.32–1.42)	0.60 (0.27–1.34)	0.18
Supplemental calcium	1.00	1.31 (0.75–2.28)	1.35 (0.73–2.48)	0.79 (0.35–1.81)		0.61
Total calcium	1.00	1.47 (0.80–2.71)	1.14 (0.59–2.22)	0.56 (0.24–1.31)	0.83(0.38 - 1.81)	0.18
Stomach cancer <sup>**</sup> (n=143)						
Dairy foods	1.00	0.61 (0.37–1.01)	$0.49\ (0.28-0.84)$	0.74 (0.46–1.19)	0.58 (0.35–0.97)	0.16
Dietary calcium	1.00	0.95 (0.58–1.56)	$0.50\ (0.28-0.91)$	0.87 (0.52–1.46)	$0.84\ (0.50{-}1.41)$	0.65
Supplemental calcium	1.00	0.81 (0.53–1.23)	1.15 (0.75–1.76)	0.54 (0.29 - 1.01)		0.20
Total calcium	1.00	0.90 (0.54–1.50)	1.37 (0.85–2.20)	0.55 (0.30–1.01)	0.71 (0.40–1.25)	0.08
Colorectal cancer <sup><math>\dot{\tau}</math>,<math>\dot{\tau}</math></sup> (n=1,635)						
Dairy foods	1.00	0.84 (0.73–0.98)	0.86 (0.74–0.99	0.78 (0.67–0.91)	0.72~(0.61-0.84)	<0.001
Dietary calcium	1.00	$0.86\ (0.74{-}1.00)$	0.81 (0.70–0.95)	0.74 (0.63–0.87)	0.70 (0.59–0.82)	<0.001
Supplemental calcium	1.00	1.02 (0.89–1.17)	0.86 (0.73–1.00)	0.86 (0.72–1.02)		0.02
Total calcium	1.00	0.87 (0.75–1.01)	0.83 (0.71–0.97)	0.71 (0.60–0.84)	$0.72\ (0.61 - 0.86)$	0.001

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Table 3

0.17

1.58 (0.78-3.20)

1.35 (0.66–2.77)

1.83 (0.93–3.58)

0.91 (0.42–1.99)

1.00

Dairy foods

			$Categories^T$			
	1	2	3	4	S	b riena
Dietary calcium	1.00	0.48 (0.21–1.11)	1.14 (0.58–2.21)	1.32 (0.68–2.55)	1.45 (0.75–2.82)	0.05
Supplemental calcium	1.00	0.50 (0.29–0.86)	0.61 (0.34–1.08)	0.42 (0.19–0.91)		0.04
Total calcium	1.00	1.38 (0.73–2.61)	1.10 (0.55–2.17)	1.05 (0.52–2.13)	0.96 (0.46–2.03)	0.60
Pancreatic cancer <sup>§§</sup> (n=384)						
Dairy foods	1.00	1.19 (0.86–1.66)	1.24 (0.89–1.72)	1.34 (0.96–1.85)	1.12 (0.80–1.58)	0.64
Dietary calcium	1.00	1.01 (0.74–1.38)	0.98 (0.71–1.35)	1.05 (0.77–1.45)	0.85 (0.60–1.20)	0.36
Supplemental calcium	1.00	0.89 (0.69–1.15)	1.02 (0.77–1.33)	0.79 (0.57–1.11)		0.34
Total calcium	1.00	1.03 (0.75–1.40)	0.93 (0.67–1.28)	0.97 (0.71–1.34)	0.88 (0.63–1.24)	0.40
Lung cancer <sup>§§</sup> (n=2,457)						
Dairy foods	1.00	0.91 (0.81–1.03)	0.86 (0.76–0.97)	0.89 (0.79–1.01)	$0.92\ (0.81 - 1.04)$	0.27
Dietary calcium	1.00	0.88 (0.78–0.99)	0.87 (0.76–0.98)	0.91 (0.80–1.03)	$0.93\ (0.81 - 1.05)$	0.48
Supplemental calcium	1.00	1.04(0.94 - 1.14)	1.03(0.92 - 1.16)	1.04 (0.92–1.19)		0.58
Total calcium	1.00	0.96 (0.85–1.08)	0.91 (0.81–1.03)	0.94 (0.83–1.07)	1.00(0.88 - 1.14)	0.95
Breast cancer <sup>////</sup> (n=5,856)						
Dairy foods	1.00	0.98 (0.90–1.06)	0.97 (0.89–1.05)	0.94~(0.87 - 1.03)	$0.96\ (0.88 - 1.04)$	0.28
Dietary calcium	1.00	0.96 (0.89–1.04)	0.95(0.87 - 1.03)	0.97 (0.89–1.05)	$0.94\ (0.86{-}1.03)$	0.28
Supplemental calcium	1.00	0.95 (0.89–1.02)	0.97 (0.90–1.04)	0.98 (0.91–1.06)		0.91
Total calcium	1.00	0.96(0.88 - 1.04)	0.95(0.87 - 1.03)	0.94 (0.86–1.02)	0.98 (0.90–1.07)	0.84
Ovarian cancer M (n=515)						
Dairy foods	1.00	1.04 (0.78–1.38)	0.94 (0.70–1.25)	1.26 (0.96–1.65)	1.03 (0.77–1.37)	09.0
Dietary calcium	1.00	1.04 (0.78–1.39)	1.05 (0.79–1.40)	1.25 (0.94–1.65)	1.02 (0.75–1.37)	0.77
Supplemental calcium	1.00	0.88 (0.70–1.10)	0.99 (0.78–1.26)	0.97 (0.74–1.27)		0.85
Total calcium	1.00	1.04 (0.78–1.38)	0.99 (0.74–1.33)	1.05 (0.79–1.41)	1.14 (0.85–1.52)	0.34
Endometrial cancer <sup>***</sup> (n=1,171)						
Dairy foods	1.00	1.19 (0.98–1.45)	1.17 (0.96–1.42)	1.22 (1.01–1.48)	1.17 (0.97–1.42)	0.27
Dietary calcium	1.00	1.09 (0.90–1.32)	1.26 (1.04–1.52)	1.06 (0.87–1.29)	1.20 (0.99–1.46)	0.18
Supplemental calcium	1.00	0.96 (0.83–1.11)	0.92(0.78 - 1.08)	0.92 (0.77–1.11)		0.35
Total calcium	1.00	1.11 (0.92–1.33)	1.01 (0.84–1.22)	1.10 (0.91–1.32)	$0.99\ (0.81 - 1.20)$	0.66
Bladder cancer $^{\dagger}\dot{\tau}\dot{\tau}$ (n=264)						
Dairy foods	1.00	1.27 (0.86–1.88)	1.24 (0.83–1.85)	1.25 (0.83–1.88)	1.45 (0.97–2.18)	0.12

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			$\mathbf{Categories}^{\check{T}}$			L
	1	2	3	4	S	p trenu
Dietary calcium	1.00	1.03 (0.70–1.52)	1.08 (0.73–1.60)	1.02 (0.68–1.54)	1.23 (0.82–1.84)	0.33
Supplemental calcium	1.00	1.17 (0.87–1.58)	0.91 (0.63–1.29)	1.03 (0.69–1.53)		0.70
Total calcium	1.00	0.97 (0.67–1.41)	0.94 (0.64–1.37)	0.91 (0.61–1.35)	0.97 (0.65–1.46)	0.85
Kidney cancer <sup>‡</sup> <sup>‡</sup> <sup>‡</sup> (n=367)						
Dairy foods	1.00	1.02 (0.72–1.45)	1.11 (0.78–1.57)	1.06 (0.75–1.51)	1.13(0.79-1.63)	0.49
Dietary calcium	1.00	$0.84\ (0.59{-}1.19)$	1.13(0.81 - 1.59)	0.77 (0.53–1.12)	1.02(0.70-1.48)	0.87
Supplemental calcium	1.00	0.93 (0.73–1.20)	$0.79\ (0.59-1.06)$	0.79 (0.57–1.12)		0.12
Total calcium	1.00	0.87 (0.63–1.21)	0.81 (0.58–1.13)	0.73 (0.51–1.03)	0.79 (0.55–1.13)	0.21
Thyroid cancer <sup>‡‡</sup> (n=199)						
Dairy foods	1.00	0.93 (0.59–1.46)	0.91 (0.58–1.44)	0.90 (0.57–1.41)	1.04 (0.67 - 1.62)	0.74
Dietary calcium	1.00	1.06 (0.69–1.64)	0.73 (0.45–1.18)	0.89 (0.57–1.41)	$1.01 \ (0.64 - 1.58)$	0.98
Supplemental calcium	1.00	1.16(0.81 - 1.66)	1.15 (0.78–1.71)	1.07 (0.68–1.68)		0.87
Total calcium	1.00	0.98 (0.63–1.54)	1.07 (0.69–1.67)	0.88 (0.55–1.41)	1.04(0.65 - 1.65)	0.98
Brain cancer <sup><math>\ddagger \pm \ddagger</math> (n=160)</sup>						
Dairy foods	1.00	0.83 (0.53–1.29)	0.45 (0.26–0.77)	0.61 (0.37 - 0.99)	0.77 (0.49 - 1.23)	0.38
Dietary calcium	1.00	0.89 (0.56–1.39)	0.56(0.34-0.94)	0.65(0.39 - 1.06)	$0.70\ (0.43{-}1.15)$	0.14
Supplemental calcium	1.00	1.03 (0.69–1.53)	1.21 (0.80–1.85)	0.84 (0.49 - 1.41)		0.67
Total calcium	1.00	$0.94\ (0.59 - 1.50)$	0.70 (0.42–1.16)	0.79 (0.48–1.29)	0.72 (0.43–1.21)	0.20
Non-Hodgkin Lymphoma‡‡ (n=660)	=660)					
Dairy foods	1.00	1.41 (1.10–1.80)	1.06(0.82 - 1.37)	1.17 (0.91–1.51)	1.00(0.77 - 1.30)	0.26
Dietary calcium	1.00	1.41 (1.11–1.81)	1.15(0.89 - 1.49)	1.06(0.81 - 1.38)	1.13 (0.87–1.47)	0.69
Supplemental calcium	1.00	0.82 (0.67–1.00)	0.95(0.77 - 1.18)	1.25 (0.99–1.56)		0.01
Total calcium	1.00	0.96 (0.75–1.23)	$0.89\ (0.69 - 1.15)$	0.99 (0.77–1.28)	1.24(0.97 - 1.59)	0.03
Leukemia‡‡ (n=280)						
Dairy foods	1.00	1.08 (0.73–1.60)	1.07 (0.72–1.59)	1.39 (0.95–2.02)	1.20 (0.81–1.77)	0.26
Dietary calcium	1.00	1.10 (0.75–1.61)	0.96(0.64 - 1.43)	1.35 (0.93–1.96)	1.13 (0.76–1.67)	0.41
Supplemental calcium	1.00	0.81 (0.60–1.09)	0.71 (0.50–1.00)	1.12 (0.79–1.57)		0.54
Total calcium	1.00	0.92 (0.63–1.35)	1.00(0.68 - 1.46)	0.92 (0.62–1.36)	1.25 (0.86–1.83)	0.17
Myeloma <sup>‡‡</sup> (n=175)						
Dairy foods	1.00	1.24 (0.76–2.01)	1.33 (0.84–2.15)	1.18 (0.72–1.95)	1.24 (0.75–2.03)	0.61

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12Dietary calcium $1.00$ $1.72 (1.03-2.86)$ Supplemental calcium $1.00$ $0.84 (0.57-1.24)$ Total calcium $1.00$ $0.84 (0.57-1.24)$ Total calcium $1.00$ $0.84 (0.57-1.24)$ Adjusted for race/ethnicity (non-Hispanic White, non-Hispanic Black, and others), enderted, not-married), body mass index (BMI, continuous), family history of cancer (erapy use (never, past, and current), alcohol consumption $(0, <5, 5-<15, 15-<30, and uncation, marital status, BMI, family history of cancer, vigorous physical activity, Dairy food and dietary and total calcium intakes were categorized according to quinti 09, 532, 648, 798 and 1101 mg/day for dietary calcium; and 494, 717, 969, 1296, and d \ge 1,000 mg/day. Dietary and supplemental calcium intakes were mutually adjusted for variables listed in the asterisked footnote + smoking status (never, forme opped <1 years ago, and currently smoking), smoking dose (0, 1-10, 11-20, 21-30, unliparous, \leq2, and \geq3 children), onal contraceptive use (never, <5, and \geq5 years), duncations, molecomy (yes, no) and hysterectomy (yes, no), and intakes of fat (quin fuintiles).$	23459 trend1.72 (103-286) $1.71 (1.02-2.87)$ $1.71 (1.01-2.88)$ $1.43 (0.83-2.49)$ $0.55$ 1.84 (0.57-1.24) $1.33 (0.91-1.95)$ $0.64 (0.37-1.11)$ $0.47$ 1.33 (0.79-224) $1.33 (0.91-1.95)$ $0.64 (0.37-1.11)$ $0.47$ 1.33 (0.79-224) $1.54 (0.93-2.57)$ $1.91 (1.16-3.15)$ $1.36 (0.79-2.36)$ $0.25$ Black, and others), education (less than high school, high school graduate, some college graduate/postgraduate/marrial status1.33 (0.79-224) $1.54 (0.93-2.57)$ $1.91 (1.16-3.15)$ $1.36 (0.79-2.36)$ $0.25$ Black, and others), education (less than high school, high school graduate, some college graduate/postgraduate/marrial status1.91 history of cancer (yes, no), vigorous physical activity (never/rarely, $\le 3$ times/month, $1-2$ , $3-4$ , and $\ge 5$ time/week), menopausal hormone5. 5- $5.5 -<15$ , $15-<30$ , and $\ge 30$ g/day), and intakes of red meat (quintiles) and total energy (continuous) and additional variables race/ethnicity,1.717, 969, 1296, and 1881 mg/day for total calcium. Supplemental calcium intake was categorized into four groups, $0, >0-<400, 400-<1,000,$ 4.717, 969, 1296, and 1881 mg/day for total calcium. Supplemental calcium intake was categorized into four groups, $0, >0-<400, 400-<1,000,$ 4.717, 969, 1296, and 1881 mg/day for total calcium. Supplemental calcium intake was categorized into four groups, $0, >0-<400, 400-<1,000,$ 4.717, 969, 1296, and 1881 mg/day for total calcium. Supplemental calcium intake was categorized into four groups, $0, >0-<400, 400-<1,000,$ 4.717, 969, 1296, and 1881 mg/day for tating smoking (never, stopped $\le 0, 4, 0.7, 1.0$ and $1.6$ servings/10	4 1.71 (1.01–2.88) 0.64 (0.37–1.11) 1.91 (1.16–3.15) ol graduate, some college, and col arrarely, ≤3 times/month, 1–2, 3–4 initiles) and total energy (continuou initiles) and total energy (continuou ential calcium intake was categorized ategory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categorized ategory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categorized in (never, stopped ≥10 years ago, serson e (never, <10 and ≥10 years), person	5 1.43 (0.83–2.49) 1.36 (0.79–2.36) lege graduate/postgraduate), mai t, and ≥5 time/week), menopausa us) and additional variables race/	p trend 0.55 0.47
Dietary calcium1.001.72 (1.03-2.86)1.71 (1.02-2.87)1.71 (1.01-2.88)1.43 (0.83-2.49)0.55Supplemental calcium1.000.34 (0.57-1.24)1.33 (0.91-1.95)0.64 (0.37-1.11)0.47Total calcium1.001.33 (0.79-2.24)1.53 (0.93-2.57)1.91 (1.16-3.15)1.56 (0.79-2.36)0.25Maried, non-micity (non-Hispanic White, non-Hispanic Black, and others), education (less than high school graduate, some college, and college graduate/postgraduate). marial statusMaried, non-marial status, BML, family history of cancer (yes, no), vigorous physical activity (never/rately, 23 time/month, 1-2, 3-4, and 25 time/wesk), menopausal hormonetherapy use (never, past, and current), alcohol consumption (0, -5, 5-61; 1530, and 250 gday), and intakes of red meat (quintiles) and total energy (continuous) and additional variables raccelhnicity,ducation, marital status, BML, family history of cancer, vigorous physical activity,ducation, marital status, BML, family history of cancer, vigorous physical activity (never/rately, 23 time/month, 1-2, 3-4, and 25 time/wesk), menopausal hormoneducation, marital status, BML, family history of cancer, vigorous physical activity,ducation, marital status, BML, family history of cancer (sec, non), vigorous physical activity (never/rately, 23 time/month, 1-2, 3-4, and 25 time/wesk), menopausal hormoneducation, marital status, BML, family history of cancer, vigorous physical activity,ducation, marital status, BML, family history of cancer (sec, non), vigorous physical activityducation, marital status, BML, family history of cancer, vigorous physical activity,ducation, marital status, BML, family history of cancer, vigorous physical act	<ul> <li>1.71 (1.02–2.87)</li> <li>1.33 (0.91–1.95)</li> <li>1.54 (0.93–2.57)</li> <li>aucation (less than high school, high schovyse, no), vigorous physical activity (nevd ≥30 g/day), and intakes of red meat (quies of the distribution. The medians for c 1.881 mg/day for total calcium. Supplem 1 in the multivariate models.</li> <li>x, and current), time since quitting smoki 31–40, 41–50, 51–60, &gt;60 cigarettes/day us tiles), fruit and vegetables (quintiles), wh</li> </ul>	1.71 (1.01–2.88) 0.64 (0.37–1.11) 1.91 (1.16–3.15) 1.91 (1.16–3.15) ol graduate, some college, and col arfrarely, $\leq 3$ times/month, 1–2, 3–4 initiles) and total energy (continuou aregory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categorizi and (never, stopped $\geq$ 10 years ago, s ng (never, stopped $\geq$ 10 years, perso- e (never, <10 and $\geq$ 10 years), perso-	<ul> <li>1.43 (0.83–2.49)</li> <li>1.36 (0.79–2.36)</li> <li>lege graduate/postgraduate), mai</li> <li>4, and ≥5 time/week), menopause</li> <li>us) and additional variables race.</li> </ul>	0.55 0.47
Supplemental calcium1.00 $0.84 (0.57-1.24)$ Total calcium $1.00$ $1.33 (0.79-2.24)$ Total calcium $1.00$ $1.33 (0.79-2.24)$ djusted for race/ethnicity (non-Hispanic White, non-Hispanic Black, and others), e arried, not-married), body mass index (BMI, continuous), family history of cancer arried, not-marrial status, BMI, family history of cancer, vigorous physical activity, Dairy food and dietary and current), alcohol consumption $(0, <5, 5-415, 15-30, and0, 532, 648, 798 and 1101 mg/day for dietary calcium; and 494, 717, 969, 1296, andd \ge 1,000 mg/day. Dietary and supplemental calcium intakes were mutually adjusteddor variables listed in the asterisked footnote + smoking status (never, formopped <1 years ago, and currently smoking), smoking dose (0, 1-10, 11-20, 21-30, ulliparous, \le2, and \ge3 children), oral contraceptive use (never, <5, and \ge5 years), duunitiles).vimber of cases$	<ul> <li>1.33 (0.91-1.95)</li> <li>1.54 (0.93-2.57)</li> <li>1.54 (0.93-2.57)</li> <li>aucation (less than high school, high school, vigorous physical activity (new d 230 g/day), and intakes of red meat (quest of the distribution. The medians for c alles are of the distribution. The medians for c alles are of the distribution of a second c alles are of the distribution of hormone replacement therapy us tiles), fruit and vegetables (quintiles), wh</li> </ul>	0.64 (0.37–1.11) 1.91 (1.16–3.15) ol graduate, some college, and col arrately, ≤3 times/month, 1–2, 3-4 initiles) and total energy (continuou initiles) and total energy (continuou ategory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categoriz ategory 1–5 were (20, 0.4, 0.7, 1.0. ental calcium intake was categoriz ategory 1–5 were (0.2, 0.4, 0.7, 1.0. ental calcium intake was categoriz ental calcium intake was categoriz ng (never, stopped ≥10 years ago, s the forwer, <10 and ≥10 years), perso	1.36 (0.79–2.36) lege graduate/postgraduate), mai 4, and ≥5 time/week), menopausa us) and additional variables race/	0.47
Total calcium1.001.33 (0.79–2.24)Adjusted for race/ethnicity (non-Hispanic White, non-Hispanic Black, and others), e aarried, not-married), body mass index (BMI, continuous), family history of cancer- erapy use (never, past, and current), alcohol consumption (0, <5, 5–	1.54 (0.93-2.57)ducation (less than high school, high schoyes, no), vigorous physical activity (new $d \ge 30$ g/day), and intakes of red meat (qules of the distribution. The medians for ciles of the distribution. The medians for c1.1881 mg/day for total calcium. Supplemin the multivariate models.sr, and current), time since quitting smokiation of hormone replacement therapy ustiles), fruit and vegetables (quintiles), wh	1.91 (1.16–3.15) ool graduate, some college, and col invitarely, $\leq 3$ times/month, 1–2, 3–4 initiles) and total energy (continuou ategory 1–5 were 0.2, 0.4, 0.7, 1.0, ental calcium intake was categoriz- ng (never, stopped $\geq 10$ years ago, s , antacid use (yes, n0), age at menc e (never, <10 and $\geq 10$ years), perso	1.36 (0.79–2.36) lege graduate/postgraduate), mar t, and ≥5 time/week), menopause us) and additional variables race.	
Adjusted for race/ethnicity (non-Hispanic White, non-Hispanic Black, and others), evarried, not-married), body mass index (BMI, continuous), family history of cancer erapy use (never, past, and current), alcohol consumption (0, $<5$ , $5-<15$ , $15-<30$ , an lucation, marital status, BMI, family history of cancer, vigorous physical activity, 2airy food and dietary and total calcium intakes were categorized according to quint 9, 532, 648, 798 and 1101 mg/day for dietary calcium; and 494, 717, 969, 1296, and $d \ge 1,000$ mg/day. Dietary and supplemental calcium intakes were mutually adjusted divided for variables listed in the asterisked footnote + smoking status (never, form opped <1 years ago, and currently smoking), smoking dose (0, 1–10, 11–20, 21–30, ulliparous, $\le2$ , and $\ge3$ children), oral contraceptive use (never, $<5$ , and $\ge5$ years), duusting the s. no), oophorectomy (yes, no) and hysterectomy (yes, no), and intakes of fat (quir uintiles).	ducation (less than high school, high scho (yes, no), vigorous physical activity (nev d 230 g/day), and intakes of red meat (qu les of the distribution. The medians for c les of the distribution. The medians for c lin the multivariate models. T, and current), time since quitting smoki 31–40, 41–50, 51–60, >60 cigarettes/day) ation of hormone replacement therapy us tiles), fruit and vegetables (quintiles), wh	ol graduate, some college, and col er/rarely, ≤3 times/month, 1–2, 3-4 initiles) and total energy (continuo ategory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categoriz, ental calcium intake was categoriz, and clower, stopped ≥10 years ago, s in antacid use (yes, no), age at menc e (never, <10 and ≥10 years), perso.	lege graduate/postgraduate), mai , and ≥5 time/week), menopausa us) and additional variables race/	0.25
Dairy food and dietary and total calcium intakes were categorized according to quinti 99, 532, 648, 798 and 1101 mg/day for dietary calcium; and 494, 717, 969, 1296, and d $\geq$ 1,000 mg/day. Dietary and supplemental calcium intakes were mutually adjusted Adjusted for variables listed in the asterisked footnote + smoking status (never, form opped <1 years ago, and currently smoking), smoking dose (0, 1–10, 11–20, 21–30, ulliparous, $\leq$ 2, and $\geq$ 3 children), oral contraceptive use (never, <5, and $\geq$ 5 years), du res, no), oophorectomy (yes, no) and hysterectomy (yes, no), and intakes of fat (quir luintiles).	les of the distribution. The medians for c 1881 mg/day for total calcium. Supplem I in the multivariate models. ar, and current), time since quitting smoki 31–40, 41–50, 51–60, >60 cigarettes/day) ation of hormone replacement therapy us tiles), fruit and vegetables (quintiles), wh	ategory 1–5 were 0.2, 0.4, 0.7, 1.0. ental calcium intake was categoriz ng (never, stopped ≥10 years ago, s , antacid use (yes, no), age at ment e (never, <10 and ≥10 years), perso		ital status I hormone ethnicity,
Adjusted for variables listed in the asterisked footnote + smoking status (never, forme opped <1 years ago, and currently smoking), smoking dose (0, 1–10, 11–20, 21–30, unliparous, $\leq$ 2, and $\geq$ 3 children), oral contraceptive use (never, <5, and $\geq$ 5 years), dunes, no), oophorectomy (yes, no) and hysterectomy (yes, no), and intakes of fat (quin quintiles). Number of cases	r, and current), time since quitting smoki 31–40, 41–50, 51–60, >60 cigarettes/day ation of hormone replacement therapy us tiles), fruit and vegetables (quintiles), wh	ng (never, stopped ≥10 years ago, s , antacid use (yes, no), age at menc e (never, <10 and ≥10 years), perso	and 1.6 servings/1000kcal/day fc ed into four groups, 0, >0-<400,	r dairy food; 400–<1,000,
Number of cases		ole grains (quintiles), total beverag	topped 5-9 years ago, stopped 1- pause(<50, 50-54, and ≥55 year nal history of diabetes (yes, no), ies (quintiles), protein (quintiles)	4 years ago, s old), parity iypertension and folate
<sup>1/</sup> Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, smoking dose, and intake of fruit and vegetables	luitting smoking, smoking dose, and intal	ke of fruit and vegetables		
Adjusted for variables listed in the asterisked footnote + smoking status, time since $c$	ng status, time since quitting smoking, smoking dose, antacid use, and intake of fruit and vegetables	ise, and intake of fruit and vegetab	les	
** Adjusted for variables listed in the asterisked footnote + smoking (never, <20 cigarettes/day in the past, >20 cigarettes/day in the past, currently<20 cigarettes/day, and currently >20 cigarettes/day), and antacid use	ettes/day in the past, >20 cigarettes/day it	the past, currently≤20 cigarettes/c	lay, and currently >20 cigarettes.	day), and
$\tau_{zz}^{\dagger}$ Adjusted for variables listed in the asterisked footnote + smoking, intakes of fruit and vegetables, whole grains, and folate.	nd vegetables, whole grains, and folate.			
$\frac{44}{3}$ Adjusted for variables listed in the asterisked footnote + smoking				
Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking, and smoking dose	quitting smoking, and smoking dose			
//// Adjusted for variables listed in the asterisked footnote + smoking, combined age at first birth and number of children, age at menopause, and intake of fat.	first birth and number of children, age at	menopause, and intake of fat.		
MM Adjusted for variables listed in the asterisked footnote + smoking, parity, oral contraceptive use, and duration of hormone replacement use.	aceptive use, and duration of hormone re	placement use.		
*** Adjusted for variables listed in the asterisked footnote + smoking, parity, and oral contraceptive use.	contraceptive use.			
747 Adjusted for variables listed in the asterisked footnote + smoking status, time since quitting smoking and smoking dose, parity, oral contraceptive use, and intakes of fruit and vegetables, and total beverages.	quitting smoking and smoking dose, parit	y, oral contraceptive use, and intak	es of fruit and vegetables, and tot	ll beverages
ttf Adjusted for variables listed in the asterisked footnote + smoking, parity, oral contraceptive use, personal history of diabetes and hypertension, and intake of protein.	raceptive use, personal history of diabete	s and hypertension, and intake of <b>p</b>	orotein.	

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