Prospective Association between Dietary Fiber Intake and Breast Cancer Risk

Mélanie Deschasaux1, Laurent Zelek1,2, Camille Pouchieu1, Mathilde His1, Serge Hercberg1,3, Pilar Galan1, Paule Latino-Martel1, Mathilde Touvier1

1 Nutritional Epidemiology Research Team, Sorbonne Paris Cité Research Center, Inserm (U557), Inra (U1125), Cnam, Paris 13 University, SMBH Paris 13, Bobigny, France, 2 Oncology Department, Avicenne Hospital, Bobigny, France, 3 Public Health Department, Avicenne Hospital, Bobigny, France

Abstract

Background: Mechanistic hypotheses suggest a potential effect of dietary fiber on breast carcinogenesis through the modulation of insulin-like growth factor bioactivity, estrogen metabolism and inflammation. An association between dietary fiber intake and breast cancer risk has been suggested in epidemiological studies but remains inconclusive. In particular, data is lacking regarding the different types of dietary fibers.

Objective: The objective was to investigate the prospective relationship between dietary fiber intake and breast cancer risk, taking into account different types of dietary fiber (overall, insoluble, soluble and from different food sources: cereals, vegetables, fruits and legumes).

Design: 4684 women from the SU.VI.MAX cohort were included in this analysis as they completed at least three 24h-dietary records within the first two years of follow-up. Among them, 167 incident invasive breast cancers were diagnosed during a median follow-up of 12.6 years (between 1994 and 2007). The associations between quartiles of dietary fiber intake and breast cancer risk were characterized using multivariate Cox proportional hazards models.

Results: Total fiber intake was not associated with breast cancer risk (HR Quartile4vs.Quartile1 = 1.29 (95%CI 0.66–2.50), P-trend = 0.5), nor was fiber intake from cereals (P-trend = 0.1), fruits (P-trend = 0.9) and legumes (P-trend = 0.3). In contrast, vegetable fiber intake was related to a decreased risk of breast cancer (HRQ4vs.Q1 = 0.50 (0.29-0.88), P-trend = 0.03). Overall vegetable intake (in g/day) was not associated with breast cancer risk (P-trend = 0.2).

Conclusion: This prospective study suggests that vegetable fiber intake may contribute to reduce breast cancer risk, in line with experimental mechanistic data.

Introduction

Several mechanisms are involved in breast cancer development. First, insulin-resistance and its consequences such as higher insulin-like growth factor [IGFs] bioactivity [1,2] or lower sex-hormone binding globulin [SHBG] [3] concentration have been associated with increased breast cancer risk in experimental [3,4] and epidemiological [3–7] studies. Second, epidemiological data suggest a relationship between breast cancer risk and increased circulating estrogens [6,8,9]. Finally, inflammation process may play a role in breast carcinogenesis, as shown in experimental [3,4,10,11] and epidemiological [12,13] studies. Mechanistic hypotheses support a role for dietary fiber in the prevention of breast cancer through a reduction of IGFs bioactivity, notably by increasing insulin-like growth factor binding protein 3 [IGFBP3] concentration [14,15]; an influence on steroid hormone concentrations by decreasing circulating estrogens [16] and upregulating SHBG concentrations [17] and a reduction of inflammation, thanks to the production of short-chain fatty acid [SCFA] by colonic fermentation [18–21].

However, epidemiological evidence is lacking. In the Continuous Update Project of the World Cancer Research Fund (WCRF) / American Institute for Cancer Research (AICR) published in 2010 [22], the expert committee stated that the epidemiological evidence regarding the association between dietary fiber intake and breast cancer risk was insufficient to conclude. Since then, two meta-analyses of prospective studies have been published, suggesting a decreased breast cancer risk associated with dietary fiber intake [23,24]. After these two meta-analyses, one prospective study, based on the EPIC cohort, has been published with similar results [25]. However, questions remain regarding the type of dietary fiber involved in this association. Different types of dietary fiber could have differential effects on breast cancer development as the definition of “dietary fiber” refers to a large category of molecules with potentially different properties and
physiological effects [26]. So far, epidemiological data remain limited and contrasted: one meta-analysis reported inverse association between soluble fiber intake and breast cancer risk, but no association with insoluble fiber intake nor with fiber intake from cereals, vegetables, fruits and legumes [24], whereas the recent large prospective EPIC study observed an inverse association between vegetable fiber intake and breast cancer risk [25]. Thus, new prospective studies considering different types of dietary fibers are needed to further investigate the relationship between dietary fiber intake and breast cancer risk.

Therefore, our objective was to prospectively investigate the association between different types of dietary fiber (overall, insoluble, soluble and from different food sources: cereals, vegetables, fruits and legumes) and breast cancer risk.

**Subjects and Methods**

**Ethics Statement**

The SU.VI.MAX study was conducted according to the Declaration of Helsinki guidelines and was approved by the Ethics Committee for Studies with Human Subjects of Paris-Cochin Hospital (CCPPRB n° 706 and n° 2364, respectively) and the Commission Nationale de l’Informatique et des Libertés (CNIL n° 33464) and n° 907094, respectively). Written informed consent was obtained from all participants.

**Subjects**

The SU.VI.MAX study (SUpplementation en VLamines et MInéraux AntioXydants) was at first designed as a randomized, double-blind, placebo-controlled primary prevention trial (Trial Registration clinicaltrials.gov Identifier: NCT00272428) aiming to assess the effect of a daily supplementation with nutritional doses of antioxidants on the incidence of cardiovascular diseases and cancers [27]. 13,017 subjects were recruited in 1994–1995 for an 8-y intervention study and were then followed for health events until September 2007.

**Baseline data collection**

At enrollment, self-administered questionnaires related to socio-demographics, smoking status, physical activity and family history of breast cancer were filled-in by all participants. Anthropometric measures were performed by the study’s nurses and physicians during a medical examination.

During the trial period (1994–2002), participants were invited to complete a 24h-dietary record every two months. These records were randomly distributed between weeks and week-ends and over seasons to take into account intra-individual variability. In order to be consistent with a prospective design, only dietary records from the first two years of follow-up were used in the present study. Completion was made through the Minitel Telematic Network, a French telephone-based terminal equivalent to an Internet prototype. Portion sizes were assessed thanks to a validated picture booklet [28] and the amounts consumed from composite dishes were estimated using French recipes validated by food and nutrition professionals. The mean daily energy, alcohol, and nutrient intakes were estimated using a published French food composition table [29]. Total dietary fiber and soluble fiber contents were obtained using the Association of Official Analytical Chemists method for total dietary fiber (AOAC 985.29) with modifications for soluble fiber measurement [30]. Dietary fiber intakes in the SU.VI.MAX study were previously described [31].

**Case ascertainment**

Health events occurring during the follow-up were self-reported by participants. Medical data were then gathered through participants, physicians, and/or hospitals and reviewed by an independent physician expert committee. Pathological reports were used to validate the cases and to extract cancer characteristics (histological type, estrogen and progesterone receptors, tumor size, number of nodes, cancer grade). Cases were classified using the International Chronic Diseases Classification, 10th Revision, Clinical Modification (ICD-10) [32]. All first incident invasive primary breast cancers were considered as cases in this study.

**Statistical analyses**

From the 7876 female participants in the SU.VI.MAX study, we excluded 120 women who reported a cancer diagnosis before the start of the follow-up. Among the remaining subjects, 4684 provided at least three valid 24h-dietary records within the first two years of follow-up and thus remained available for analysis. For overall breast cancer analysis, women contributed person-time until the date of diagnosis of breast cancer, the date of last completed questionnaire, the date of death, or September 2007, whichever occurred first. For analyses stratified by menopausal status, women contributed person-time until their date of menopause for premenopausal breast cancer analysis or from their date of menopause for postmenopausal breast cancer analysis. Women who reported a cancer other than breast cancer (N = 164) or a non-invasive breast cancer (N = 23) during the study period were included and censored at the date of diagnosis (except basal cell skin carcinoma, not considered as cancer). Nutrient intakes were estimated by the average intake calculated from all dietary records for each woman.

Baseline characteristics of participants were compared between quartiles of total dietary fiber intake, using Chi-square tests or Fisher tests where appropriate. Hazard ratios (HRs) and 95% Confidence Intervals (CIs), obtained from Cox proportional hazards models with age as the primary time variable, were used to characterize the association between quartiles of dietary fiber intake and incident breast cancer. We verified that the assumptions of proportionality were satisfied through examination of the log-log (survival) versus log-time plots. Different categories of dietary fibers were tested: according to their chemical properties (soluble and insoluble fibers) and according to their food sources (cereal, vegetable, fruit and legume fibers). Tests for linear trend were performed using the ordinal score on quartiles of fiber intake. Multivariate models were adjusted for intervention group of the initial SU.VI.MAX trial (yes/no), smoking status (never, former or current), educational level (primary, secondary or university), physical activity (irregular, <1h/d or ≥1h/d walking or equivalent), height (continuous), body mass index (BMI; continuous), without-alcohol energy intake (continuous), alcohol intake (continuous), total fat intake (continuous), number of dietary records (continuous), family history of breast cancer (yes/no), number of children (continuous), menopausal status at baseline (yes/no) and use of hormonal treatment for menopause (HTM) at baseline (yes/no). Since a high fiber intake might reflect an overall healthy diet and since we aimed at disentangling the potential effect of dietary fiber from the effect of other components of a healthy diet, we adjusted the multivariate models for a healthy dietary pattern. This healthy pattern was extracted by principal component analysis, using the SAS “proc factor” procedure with the “Varimax” option, from mean intakes across all 24-h records collected during the first 2 years of the study, for 31 food groups. For interpreting the data, we considered food groups with a factor loading under −0.2 or over 0.2. The factor that was strongly
with a decreased breast cancer risk (HR Q4 vs. Q1 = 0.50 (0.29-0.88), trend = 0.3). In contrast, vegetable fiber intake was associated with breast cancer risk (HR Q4 vs. Q1 = 0.42 (0.21–0.83), P-trend = 0.02), ER+ (n = 113, HR Q4 vs. Q1 = 0.37 (0.18–0.76), P-trend = 0.02) and PR+ (n = 86, HR Q4 vs. Q1 = 0.36 (0.16–0.81), P-trend = 0.046) breast cancers (data not tabulated).

Quartiles of overall vegetable intake (g/d) were not associated with breast cancer risk (P-trend = 0.2, data not tabulated). Results regarding legume fibers (no association with breast cancer risk) were similar when excluding soya and soya products from the legume food group (data not shown). No interaction between fiber intake and BMI was detected (data not shown).

Sensitivity analyses excluding incident breast cancer cases diagnosed within the first two years of follow-up did not modify the findings (146 cases, out of 4663 included women), nor did sensitivity analyses including only women who completed at least six 24h-dietary records during the first two years of follow-up (cases = 158, out of 3771 included women) or including women who provided at least one 24h-dietary record (cases = 204, out of 5710 included women). We also performed analyses considering dietary fiber intake as a time-dependent variable with one averaged value of intake per year of follow-up (number of included cases = 204, out of 5710 included women). Again, this did not modify our findings (data not shown).

### Discussion

In this prospective study, we observed an inverse association between vegetable fiber intake and breast cancer risk, but no association with total dietary fiber intake or fiber intake from other food sources.

The two recently published meta-analyses [23,24], as well as the subsequent prospective study on the EPIC cohort [25] observed an inverse association between total dietary fiber and breast cancer risk. However, this association was borderline significant in the EPIC cohort study (P_trend = 0.03 but HR Q5-Q1 = 0.95 (0.89, 1.01)). The fact that we did not observe any association between total dietary fiber and breast cancer risk in our study may be explained by lack of statistical power, and insufficient contrast between compared quartiles of dietary fiber intake. Indeed, in the recent meta-analysis published by Aune et al. [24], the inverse association between total dietary fiber intake and breast cancer risk was only observed among studies with a large range (>15 g/day) or high level of intake (>25 g/day) in stratified analyses. In our study population, the proportion of women who reached 25 g/day of total dietary fiber was low (only 8.6%).

The meta-analysis of Aune et al. [24] did not detect statistically significant association between fiber intake from different food groups and breast cancer risk. In contrast, our result of an inverse association between vegetable fiber intake and breast cancer risk was consistent with the findings observed in one recent case-control study [36] and in the large recent prospective EPIC study [25], where vegetable fibers were the only fiber subtype associated with decreased breast cancer risk. Additional epidemiological studies including wide ranges of fiber intakes from each food source and assessing precisely these intakes are needed to more thoroughly elucidate the associations between each type of fiber and breast cancer risk.

In this study, overall vegetable intake (in g/d) was not associated with breast cancer risk, which supports a specific effect of vegetable fiber in breast cancer prevention. In addition, we adjusted for a healthy dietary pattern and for several lifestyle factors (e.g. physical activity, smoking status, etc.). Thus, the inverse association observed in the present study between vegetable fiber intake and breast cancer risk could not be entirely explained by a more general effect of vegetable intake or overall dietary/lifestyle pattern.

Mechanistic data support the plausibility of a protective effect of dietary fiber on breast carcinogenesis, especially vegetable fiber. Vegetable fibers combine insoluble (cellulose) and soluble (pectic substances) fibers [37,38] in equal proportions. A similar 1:1 combination of soluble and insoluble fibers (psyllium and wheat bran) has been shown to be efficient in the protection against mammary tumorigenesis in rats [39].

The decrease of circulating estrogen concentration by dietary fibers [16,40] may result at least in part from a modified enterohepatic circulation of estrogens [41,42], through decrease in the colonic β-D-glucuronidase activity [39,43], an enzyme allowing estrogens to re-enter the circulation [39,43], and binding to estrogens, resulting in increased fecal excretion [40,41]. The influence of dietary fiber on estrogen metabolism may vary according to their biochemical properties (e.g., solubility, fermentability and/or ionic exchange capacity).

Fermentation of dietary fibers in the colon produces SCFA [44], in particular butyrate [45] and propionate [46], which enter the circulation [47] and may exert an anti-inflammatory role [20,48]. Vegetable fibers provide on average 76% acetate, 14% propionate and in particular butyrate [45] and propionate [46], which enter the circulation [47] and may exert an anti-inflammatory role [20,48]. Vegetable fibers combine insoluble (cellulose) and soluble (pectic substances) fibers [37,38] in equal proportions. A similar 1:1 combination of soluble and insoluble fibers (psyllium and wheat bran) has been shown to be efficient in the protection against mammary tumorigenesis in rats [39].

The decrease of circulating estrogen concentration by dietary fibers [16,40] may result at least in part from a modified enterohepatic circulation of estrogens [41,42], through decrease in the colonic β-D-glucuronidase activity [39,43], an enzyme allowing estrogens to re-enter the circulation [39,43], and binding to estrogens, resulting in increased fecal excretion [40,41]. The influence of dietary fiber on estrogen metabolism may vary according to their biochemical properties (e.g., solubility, fermentability and/or ionic exchange capacity).

Fermentation of dietary fibers in the colon produces SCFA [44], in particular butyrate [45] and propionate [46], which enter the circulation [47] and may exert an anti-inflammatory role [20,48]. Vegetable fibers combine insoluble (cellulose) and soluble (pectic substances) fibers [37,38] in equal proportions. A similar 1:1 combination of soluble and insoluble fibers (psyllium and wheat bran) has been shown to be efficient in the protection against mammary tumorigenesis in rats [39].
Table 1. Baseline characteristics of the women (N = 4684) according to quartiles of total fiber intake, SU.VI.MAX cohort, France, 1994–2007.

|                       | Q1 (n = 1171) | Q2 (n = 1171) | Q3 (n = 1171) | Q4 (n = 1171) | P*  |
|-----------------------|--------------|--------------|--------------|--------------|-----|
| Age (years)           | 46.6         | 46.6         | 47.1         | 47.6         | 0.0001 |
| BMI (kg/m²)           | 23.4         | 23.0         | 23.0         | 23.0         | 0.005 |
| ≥25 kg/m²             | 306 (26.1)   | 242 (20.7)   | 246 (21.0)   | 246 (21.0)   | 0.003 |
| Height (cm)           | 161 ± 6.0    | 161 ± 5.9    | 162 ± 5.7    | 163 ± 5.9    | 0.0001 |
| Intervention group (yes) | 552 (47.1)  | 569 (48.6)   | 602 (51.4)   | 594 (50.7)   | 0.1  |
| Smoking status        |              |              |              |              | 0.0001 |
| Never                 | 594 (50.7)   | 671 (57.3)   | 700 (59.8)   | 739 (63.1)   |      |
| Former                | 329 (28.1)   | 327 (27.9)   | 353 (30.2)   | 338 (28.9)   |      |
| Current               | 248 (21.2)   | 173 (14.8)   | 118 (10.1)   | 94 (8.0)     |      |
| Physical activity     |              |              |              |              | 0.0001 |
| Irregular             | 347 (29.6)   | 312 (26.6)   | 295 (25.2)   | 245 (20.9)   |      |
| <1h/d walking or equivalent | 367 (31.3) | 406 (34.7)   | 428 (36.6)   | 435 (37.2)   |      |
| ≥1h/d walking or equivalent | 457 (39.0) | 453 (38.7)   | 448 (38.3)   | 491 (41.9)   |      |
| Educational level     |              |              |              |              | 0.0001 |
| Primary               | 271 (23.1)   | 196 (16.7)   | 204 (17.4)   | 181 (15.5)   |      |
| Secondary             | 454 (38.8)   | 469 (40.1)   | 466 (39.8)   | 456 (38.9)   |      |
| University            | 446 (38.1)   | 506 (43.2)   | 501 (42.8)   | 534 (45.6)   |      |
| Family history of breast cancer (yes, %) | 104 (8.9) | 108 (9.2) | 110 (9.4) | 85 (7.3) | 0.2 |
| Number of children    | 2 ± 1.1      | 2 ± 1.1      | 2 ± 1.1      | 2 ± 1.2      | 0.6  |
| Menopausal status at baseline (yes, %) | 337 (28.8) | 341 (29.1) | 358 (30.6) | 377 (32.2) | 0.3 |
| Age at menopause (years) | 51.0 ± 4.7  | 51.1 ± 4.3   | 50.9 ± 4.2   | 51.2 ± 3.9   | 0.4  |
| Use of HTM at baseline (yes, %) | 317 (27.1) | 330 (28.2) | 375 (32.0) | 366 (31.3) | 0.02 |
| Energy intake (kcal/d) | 1438.3 ± 367.6 | 1746.2 ± 345.5 | 1934.7 ± 363.9 | 2188.9 ± 446.3 | 0.0001 |
| Alcohol intake (g/d)  | 11.9 ± 15.8  | 11.3 ± 13.0  | 10.9 ± 12.7  | 8.8 ± 10.8   | 0.006 |
| Total fat intake (g/d) | 63.9 ± 19.9  | 76.8 ± 18.9  | 84.2 ± 19.9  | 93.9 ± 25.2  | 0.0001 |
| Total dietary fiber intake (g/d) | 10.7 ± 2.0  | 15.0 ± 0.9   | 18.4 ± 1.1   | 24.9 ± 4.9   | 0.0001 |
| Insoluble fiber (g/d) | 8.4 ± 1.7    | 11.9 ± 0.9   | 14.6 ± 1.0   | 19.9 ± 4.1   | 0.0001 |
| Soluble fiber (g/d)   | 2.3 ± 0.5    | 3.1 ± 0.5    | 3.8 ± 0.6    | 5.0 ± 1.2    | 0.0001 |
| Cereal fiber (g/d)    | 4.1 ± 1.4    | 5.6 ± 1.7    | 6.7 ± 2.0    | 8.7 ± 3.3    | 0.0001 |
| Vegetable fiber (g/d) | 2.7 ± 1.2    | 3.6 ± 1.4    | 4.4 ± 1.6    | 5.7 ± 2.2    | 0.0001 |
| Fruit fiber (g/d)     | 2.0 ± 1.3    | 3.2 ± 1.5    | 4.1 ± 1.8    | 5.8 ± 2.9    | 0.0001 |
| Legume fiber (g/d)†   | 0.5 ± 0.7    | 0.7 ± 0.9    | 1.1 ± 1.2    | 1.7 ± 2.0    | 0.0001 |
| Score of overall healthy dietary pattern | −0.6 ± 0.8 | −0.2 ± 0.8  | 0.1 ± 0.8    | 0.7 ± 1.0    | 0.0001 |

BMI body mass index; HTM hormonal treatment for menopause; Q Quartile. Values are mean ± SD for all variables except for BMI ≥25 kg/m², intervention group, smoking status, physical activity, educational level, family history of breast cancer, menopausal status at baseline and use of HTM at baseline for which they are N, %.

*Chi-square tests or Fisher tests as appropriate. Data for dietary variables were log-transformed to improve normality. All statistical tests were 2-sided.

†Among first degree relatives.

Including fiber from soya and soya products.

doi:10.1371/journal.pone.0079718.t001

Strengths of our study pertained to its prospective design with long follow-up and to the diversity of types and sources of dietary fibers investigated. Moreover, the precise assessment of dietary fiber intake through repeated 24h-dietary records (at least 3, mean = 9.2 ± 3.4) also represents a strength compared to studies that used a food frequency questionnaire (FFQ), which is known to provide a good classification of subjects but a less precise estimation of dietary (and thus fiber) intake and an attenuation of the estimated relative risks [49]. Indeed, a recent prospective study on dietary fiber and colorectal cancer risk compared two dietary assessment tools, i.e., food diaries and FFQ within the same study population and observed statistically significant associations only when dietary fiber was measured by food diaries [50].

However, some limitations should be considered. First, although the number of overall breast cancer cases was reasonably large, it did not allow us to investigate all histological and receptor types of breast cancers (apart from the main subtypes, i.e., postmenopausal, ductal and ER+ or PR+). Nevertheless, even if our ability to detect some of the hypothesized observations may have been limited by the number of cases, this is unlikely to explain the observed relationships which were statistically significant despite the potential power limitation. Second, our results could also have been affected by residual or unmeasured confounding. However, a
References

Table 2. Associations between quartiles of dietary fiber intake and breast cancer risk from multivariate Cox proportional hazards models1, SU.VI.MAX cohort, France, 1994–2007 (167 cases /4684 women).

| Dietary fiber | Q1 HR | Q2 HR | 95% CI | Q3 HR | 95% CI | Q4 HR | 95% CI | P for trend |
|---------------|------|------|--------|------|--------|------|--------|------------|
| Total fiber   | 1.19 | 0.73–1.93 | 1.18 | 0.69–2.03 | 1.29 | 0.66–2.50 | 0.5 |
| Insoluble fiber | 1.22 | 0.75–1.99 | 1.29 | 0.75–2.22 | 1.32 | 0.68–2.57 | 0.4 |
| Soluble fiber | 1.12 | 0.70–1.81 | 1.12 | 0.67–1.87 | 1.22 | 0.67–2.22 | 0.6 |
| Cereal fiber | 1.05 | 0.64–1.72 | 1.44 | 0.88–2.38 | 1.43 | 0.81–2.53 | 0.1 |
| Vegetable fiber | 0.83 | 0.54–1.28 | 0.83 | 0.53–1.30 | 0.50 | 0.29–0.88 | 0.028 |
| Fruit fiber | 0.92 | 0.58–1.45 | 0.86 | 0.54–1.39 | 1.07 | 0.64–1.79 | 0.9 |
| Legume fiber | 1.63 | 1.03–2.59 | 1.25 | 0.77–2.04 | 1.44 | 0.90–2.31 | 0.3 |

HR Hazard Ratio; CI Confidence Interval; Q Quartile.

1 Adjusted for age (time interval), intervention group, smoking status, educational level, physical activity, height, BMI, number of dietary records, without-alcohol energy intake, alcohol intake, total fat intake, overall healthy dietary pattern, family history of breast cancer, menopausal status at baseline, use of HTM and number of children.

Cut-offs (g/d) for quartiles of dietary fiber intakes were 13.3/16.6/20.3 for total fiber, 10.5/13.2/16.2 for insoluble fiber, 2.7/3.4/4.2 for soluble fiber, 4.4/5.9/7.7 for cereal fiber, 2.7/3.8/5.2 for vegetable fiber, 2.1/3.4/5 for fruit fiber and 0.05/0.5/1.4 for legume fiber.

doi:10.1371/journal.pone.0079718.t002

Acknowledgments

The authors thank Gwenael Monot, Yvonne Essedhlik, Paul Flanzy, Mohand Ait Ouifella, Yasmin Cherghous, and Than Duong Van (computer scientists), Florence Charpentier (dietitian), Nathalie Arnault, Veronique Gourlet, Fabien Szabo, Laurent Bourhis, and Stephen Besseu (statisticians), and Rachida Mehroug (logistics assistant) for their technical contribution to the SU.VI.MAX study.

Author Contributions

Conceived and designed the experiments: MD MT. Analyzed the data: MD MT. Contributed reagents/materials/analysis tools: LZ CP MH SH PG PLM MT. Wrote the paper: MD MT. Acquired the data: SH PG LZ.

References

1. Godsland IF (2010) Insulin resistance and hyperinsulinaemia in the development and progression of cancer. Clin Sci (Lond) 118: 313–332.

2. Kaaks R, Lukekawa A (2001) Energy balance and cancer: the role of insulin and insulin-like growth factor-I. Proc Nutr Soc 60: 91–106.

3. Arcidiacono B, Iritano S, Nocera A, Possidente K, Nevolo MT et al. (2012) Insulin resistance and cancer risk: an overview of the pathogenetic mechanisms. Exp Diabetes Res 2012: 709174.

4. Sung MK, Yeon JY, Park SY, Park JH, Choi MS (2011) Obesity-induced metabolic stresses in breast and colon cancer. Ann N Y Acad Sci 1229: 61–68.

5. Renuhan AG, Zawalsh M, Minder C, O’Dwyer ST, Shalot SM et al. (2004) Insulin-like growth factor (IGF)-I, IGF binding protein-3, and cancer risk: systematic review and meta-regression analysis. Lancet 363: 1346–1353.

6. Key T, Appleby P, Barnes I, Reeves G (2002) Endogenous sex hormones and breast cancer in postmenopausal women: reanalysis of nine prospective studies. J Natl Cancer Inst 94: 606–616.

7. Key TJ, Appleby PN, Reeves GK, Roddam AW (2010) Insulin-like growth factor I (IGF1), IGF binding protein 3 (IGFBP3), and breast cancer risk: pooled individual data analysis of 17 prospective studies. Lancet Oncol 11: 530–542.

8. Key TJ (2011) Endogenous oestrogens and breast cancer risk in premenopausal and postmenopausal women. Steroids 76: 812–815.

9. Walker K, Bratton DJ, Frost C (2011) Premenopausal endogenous oestrogen levels and breast cancer risk: a meta-analysis. Br J Cancer 105: 1451–1457.

10. Khudrakar MJ, Cohen P, Spiegelman BM (2011) Molecular mechanisms of cancer development in obesity. Nat Rev Cancer 11: 896–903.
Dethlefsen C, Hofjeldt G, Hojman P (2013) The role of intratumoral and systemic IL-6 in breast cancer. Breast Cancer Res Treat 138: 657–664.

Touvier M, Fezeu L, Ailhaud N, Julia C, Chaix N et al. (2013) Association between prediagnostic biomarkers of inflammation and endothelial function and cancer risk: a nested case-control study. Am J Epidemiol 177: 3–13.

Gross A, Newshaffer CJ, Hoffman Bolton JA, Rifa N, Visvanathan K (2013) Adipocytokines, Inflammation, and Breast Cancer Risk in Postmenopausal Women: A prospective study. Cancer Epidemiol Biomarkers Prev.

Ferrari P, Rinaldi S, Jenab M, Lukanova A, Olsen A et al. (2013) Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies. Am J Epidemiol 177: 1257–1267.

Hercberg S, Chat-Yung S, Chaulac M (2008) The French National Nutrition and Health Program: 2001-2006/2010. Int J Public Health 53: 68–77.

Zhang CX, He SC, Cheng SZ, Chen YM, Fu JH et al. (2011) Effect of dietary fiber intake on breast cancer risk according to estrogen and progesterone receptor status. Eur J Clin Nutr 65: 899–906.

Andersson JW, Smith BM, Gustafson NJ (1994) Health benefits and practical aspects of high-fiber diets. Am J Clin Nutr 59: 1248–1248.

Bourquin DP, Tjigemeyer EG, Fahey GC, Jr. (1993) Vegetable fiber fermentation by human fecal bacteria: cell wall polysaccharide disappearance and short-chain fatty acid production during in vitro fermentation and water-holding capacity of unfermented residues. J Nutr 123: 860–869.

Cohen LA, Zhao Z, Zang EA, Wynn TT, Simi B et al. (1996) Wheat bran and psyllium effects: effects on N-methyl-N-nitosourea-induced mammary tumorigenesis in F344 rats. J Natl Cancer Inst 88: 899–907.

Moore MA, Park CB, Tsaoda H (1998) Soluble and insoluble fiber influences on cancer development. Crit Rev Oncol Hematol 27: 229–242.

Aubertin-Leheudre M, Gorbach S, Woods M, Drewt JT, Goldin B et al. (2008) Fat/fiber intakes and sex hormones in healthy premenopausal women in USA. J Steroid Biochem Mol Biol 112: 32–39.

Willett WC (2001) Diet and breast cancer. J Intern Med 249: 395–411.

Gerber M (1996) Fiber and breast cancer: another piece of the puzzle—but still an incomplete picture. J Natl Cancer Inst 88: 899–907.

Dahm CC, Keogh RH, Spencer EA, Greenwood DC, Key TJ et al. (2010) Dietary fiber and colorectal cancer risk: a nested case-control study using food diaries. J Natl Cancer Inst 102: 614–626.

Nicola AC, Ostman EM, Knudsen KE, Holst JJ, Bjorck IM (2010) A cereal-based evening meal rich in indigestible carbohydrates increases plasma butyrate the next morning. J Nutr 140: 1932–1936.

King DE, Elgan BM, Woolson RF, Mainous AG, III, Al-Soliman Y et al. (2007) Effect of a high-fiber diet vs a fiber-supplemented diet on C-reactive protein level. Arch Intern Med 167: 502–506.

Schatzkin A, Kipnis V, Carroll RJ, Midthune D, Subar AF et al. (2003) A comparison of a food frequency questionnaire with a 24-hour recall for use in an epidemiological cohort study: results from the biomarker-based Observing Protein and Energy Nutrition (OPEN) study. Int J Epidemiol 32: 1054–1062.

Dahm CC, Keogh RH, Spencer EA, Greenwood DC, Key TJ et al. (2010) Dietary fiber and colorectal cancer risk: a nested case-control study using food diaries. J Natl Cancer Inst 102: 614–626.

Dubuisson C, Léoret S, Touvier M, Dufour A, Calamassi-Tran G et al. (2010) Trends in food and nutritional intakes of French adults from 1999 to 2007: results from the INCA surveys. Br J Nutr 103: 1035–1048.

Belle FN, Kampman E, McKenna A, Bernstein L, Reaven PD et al. (2003) Fat/fiber intakes and sex hormones in healthy premenopausal women in USA. J Steroid Biochem Mol Biol 112: 32–39.