Evaluation of Publicly Available Scientific Evidence Regarding Certain Nutrient-Disease Relationships:

5. Dietary Fiber and Cancer

December 1991

By
David Kritchevsky, Ph.D.

Prepared for

CENTER FOR FOOD SAFETY AND APPLIED NUTRITION
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20204

under

FDA Contract No. 223-88-2124
Task Order #9

LIFE SCIENCES RESEARCH OFFICE
FEDERATION OF AMERICAN SOCIETIES
FOR EXPERIMENTAL BIOLOGY
9650 Rockville Pike
Bethesda, MD 20814-3998
EVALUATION OF PUBLICLY AVAILABLE
SCIENTIFIC EVIDENCE REGARDING
CERTAIN NUTRIENT–DISEASE RELATIONSHIPS:

5. DIETARY FIBER AND CANCER

December, 1991
By
David Kritchevsky, Ph.D.

Prepared for
CENTER FOR FOOD SAFETY AND APPLIED NUTRITION
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20204

under
FDA Contract No. 223–88–2124
Task Order #9

Life Sciences Research Office
Federation of American Societies
For Experimental Biology
9650 Rockville Pike
Bethesda, Maryland 20814
FOREWORD

The Life Sciences Research Office (LSRO), Federation of American Societies for Experimental Biology (FASEB), provides scientific assessments of topics in the biomedical sciences. Reports are based upon literature reviews and the scientific analyses of knowledgeable investigators engaged in work in specific areas of biology and medicine.

This report was developed for the Center for Food Safety and Applied Nutrition, Food and Drug Administration (FDA), in accordance with the provisions of Task Order #9 of Contract No. 223-88-2124. Potential authors and reviewing consultants were identified by the LSRO based on their qualifications, experience, and freedom from conflict of interest, with due consideration for balance and breadth in appropriate disciplines. The author and reviewing consultants were selected with the concurrence of the LSRO Advisory Committee (which consists of representatives of each constituent Society of FASEB).

On March 14, 1991, the FDA requested submission of scientific data and information on the ten specific topics for which health claims might be made (Federal Register 56:12932-12933). The scientific data and information provided in response to this request were considered by LSRO in preparing this report. Copies of the submitted materials are available for public inspection at the Dockets Management Branch, FDA (Docket No. 91N-0098). Copies of documents cited in this report are available for public inspection at LSRO, FASEB.

David Kritchevsky, Ph.D., Associate Director, Wistar Institute, Philadelphia, PA should be cited as the author of this report. The LSRO acknowledges the efforts of David Kritchevsky, Ph.D. and also the critical assistance of Elizabeth L. Barrett-Connor, M.D., Professor of Medicine and Community Medicine, University of California, San Diego, CA; Barbara O. Schneeman, Ph.D., Professor and Chairman, Department of Nutrition, University of California, Davis, CA; and Jon A. Story, Ph.D., Professor, Department of Foods and Nutrition, Purdue University, West Lafayette, IN, who reviewed several drafts of the manuscript. The appendix tables were prepared by the LSRO staff and author and were critically reviewed by the author and reviewers. Subsequently the draft report and tables were revised by the author, edited by the LSRO scientific staff, and received final concurrence from the author and reviewing consultants.

The evaluation of scientific literature, data, and information submitted to the LSRO was made by the author, reviewers, and the LSRO independently of FDA or any other group, governmental or non-governmental. The author and LSRO accept responsibility for the accuracy of the report conclusions and its appendix table(s). This final report was reviewed and approved by members of the LSRO Advisory Committee under authority delegated by the Federation Board. The LSRO Advisory Committee members who reviewed this report were free of conflicts of interest in regard to the subject matter under policies established by the Federation. Upon completion of these review procedures, the report was approved by the Executive Director, FASEB, and transmitted to FDA.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of each individual member of the FASEB constituent Societies.

______________________________
December 31, 1991
Date

Kenneth D. Fisher, Ph.D.
Director
Life Sciences Research Office
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOREWORD</td>
<td>iii</td>
</tr>
<tr>
<td>I. INTRODUCTION</td>
<td>1</td>
</tr>
<tr>
<td>A. Background Information</td>
<td>1</td>
</tr>
<tr>
<td>1. Definition</td>
<td>1</td>
</tr>
<tr>
<td>2. Analysis</td>
<td>2</td>
</tr>
<tr>
<td>3. Diet–cancer relationships</td>
<td>2</td>
</tr>
<tr>
<td>B. Objective and Scope</td>
<td>2</td>
</tr>
<tr>
<td>II. DIETARY FIBER AND CANCER</td>
<td>5</td>
</tr>
<tr>
<td>A. Human Studies</td>
<td>5</td>
</tr>
<tr>
<td>1. Colon cancer</td>
<td>5</td>
</tr>
<tr>
<td>2. Breast cancer</td>
<td>8</td>
</tr>
<tr>
<td>3. Other cancers</td>
<td>8</td>
</tr>
<tr>
<td>4. Conclusion</td>
<td>9</td>
</tr>
<tr>
<td>B. Animal and Biomedical Studies</td>
<td>9</td>
</tr>
<tr>
<td>1. Animal studies</td>
<td>9</td>
</tr>
<tr>
<td>2. Biomedical studies of markers of colon</td>
<td>10</td>
</tr>
<tr>
<td>3. Cancer risk</td>
<td>10</td>
</tr>
<tr>
<td>C. Discussion</td>
<td>10</td>
</tr>
<tr>
<td>1. Dietary interactions</td>
<td>10</td>
</tr>
<tr>
<td>2. Summary of certain associated factors</td>
<td>11</td>
</tr>
<tr>
<td>3. Overall summary</td>
<td>13</td>
</tr>
<tr>
<td>D. General Conclusions</td>
<td>14</td>
</tr>
<tr>
<td>III. BIBLIOGRAPHY</td>
<td>17</td>
</tr>
<tr>
<td>APPENDIX</td>
<td>A-1</td>
</tr>
</tbody>
</table>
I. INTRODUCTION

A. BACKGROUND INFORMATION

The importance of dietary fiber components in the diet has been recognized for many years but has received increased attention in the past 12 to 15 years. Study of the role of dietary fiber in health and disease was stimulated by the work of Burkitt (1971, 1973a,b) and Painter et al. (1972). These and other investigators hypothesized that the relatively low level of plant fiber in the diets of Western societies predisposed these populations to disease and disorders which differ from those in less developed regions. Interest in this hypothesis has led to a number of laboratory, clinical, and epidemiological studies, suggestions for health benefits of dietary fiber, development of new food products and diets, calls for guidelines on the fiber content and labeling of food products, and revision of nutritional recommendations. However, dietary fiber intake is only one aspect that must be considered in making dietary recommendations and is difficult to address in isolation from the total diet.

Various beneficial health effects have been suggested for dietary fiber, individual components of dietary fiber, and fiber-containing foods. Epidemiological studies and/or clinical trials have been conducted to examine the effects of fiber on glycemic response, lipid metabolism, laxation, diverticular disease, colon cancer, weight loss, and many other conditions. Interpretation of these studies is complicated by differences in the methods used for assessing dietary fiber intake in epidemiological studies and differences in the type and level of fiber components and fiber-containing foods used in clinical trials. The same factors also complicate studies of the potential adverse effects of high amounts of dietary fiber, e.g., altered availability of minerals and trace elements, altered absorption of drugs, changes in bowel function, and others.

1. Definition

Despite increasing public and scientific interest, several problems have impeded research on the health effects of dietary fiber. One major issue has been the absence of a universally accepted definition of dietary fiber. Most definitions encompass a wide variety of compounds with different chemical characteristics and physiological functions.

While the term "crude fiber" has been used for several decades, a universally acceptable definition of dietary fiber has not been achieved. A classification for dietary products and foods was submitted at the XIII International Congress of Nutrition (Spiller and Jenkins, 1986). Four groupings were presented:

a) Whole foods high in fiber,
b) A high-fiber fraction (such as wheat bran) which could be produced without affecting the structure and/or composition of the material as present in the food,
c) Concentrated fibers, such as pectin or cellulose, which have been altered in the course of extraction from food sources and subsequent purification, and
d) Fiber-enriched foods
Each of these types of product may contain the same amount of a given fiber, but the action of that fiber will be affected by its physical form and by other substances in the food. For example, is the fiber added to a semi-purified diet the same as that fiber in its natural milieu? Is it the same in steric form? Are its interactions with other dietary components the same?

2. **Analysis**

As might be expected from the diverse chemical constituents, no one analytical methodology has been entirely satisfactory for identification and characterization of the many components of dietary fiber from all sources.

The analysis of dietary fiber is a field still in flux. Marlett (1990) has addressed this problem which has no solution as yet because there are no universally accepted methods of analysis which are based on universally accepted definitions. One major problem lies in the fact that the fiber is an integral part of the foodstuff being analyzed and some of the fiber may be "masked" by its association with other components and nutrients. For example, Marlett et al. (1989) demonstrated that the recovery of soluble fiber is a function of methodology. Thus, pre-treatment with pepsin raises the yield of soluble fiber (percent dry wt. of food) by 48 percent in peas, 71 percent in kidney beans, and 15 percent in oat bran.

The designations of dietary fiber as soluble and insoluble fibers are facile but not totally accurate. Almost all fibers occurring in food are a mixture of the insoluble fibers such as cellulose and hemicellulose and gelling fibers such as pectin. Fibers such as pectin do not form true gels but do increase the viscosity of aqueous solutions. The soluble fibers tend to form gels (pectin, gums) rather than dissolve, as the designation suggests. Thus we are labeling materials by their major component but not total composition, which may be misleading. In general, the brans (wheat, rice, corn, oat) are considered as insoluble fibers but the hypocholesterolemic properties of oat bran are due to its appreciable content of oat gum (β-glucan). An issue that may require more clarification is that food fibers are mixtures whose identity depends in part on analytical methodology used for their identification.

3. **Diet–cancer relationships**

While the overall area of diet and cancer has been of medical concern for many years, intense interest in the lay and medical communities can be dated to 1981 when an exhaustive review by Doll and Peto suggested that 35 percent of cancer deaths (range 10–70 percent) in the U.S. could be attributed to diet. A few years later Peto (1986) reproduced the table which had appeared in the 1981 publication with the heading "Future Perfect" suggesting what might be found in the future. In an accompanying table labeled "Present Imperfect" attribution of cancer causation to diet was revised downward drastically. Instead of suggesting that 35 percent of cancer deaths could be attributable to diet, the figure was 1 percent. In 1986, Higginson and Oettlé suggested that the virtual absence of large bowel cancer in black Africans might be due to an aspect of their diet, specifically dietary bulk. Burkitt (1971) attributed differences in incidence of colon cancer between African and Western populations to dietary fiber intake. Comparisons of fiber intake in populations are really comparisons of fiber–rich foods which contain a number of other materials (carotene, selenium, etc.) which may influence tumorigenesis.
B. OBJECTIVE AND SCOPE

This review considers the weight of scientific evidence that relates dietary fiber to occurrence of various types of cancer. It reviews and evaluates the literature published since 1987 on relationships between dietary fiber and cancer and compares the conclusions reached with those of previously published exemplary reviews. This review focuses principally on colon and breast cancer in relation to dietary fiber and considers the results of case-control, epidemiologic, and prospective studies of human subjects. Animal studies are cited only when they contribute significantly to understanding the mechanisms of fiber effects in causation of cancer. The review is a component of a series of reports on the interrelationships of dietary components and nutrients with various human diseases.
II. DIETARY FIBER AND CANCER

A number of noteworthy expert reviews have evaluated and summarized the recent literature on relationships between dietary fiber and cancer; for example, Diet and Health (1989), the National Research Council Committee on Diet, Nutrition and Cancer (NRC, 1982), Peto (1986), the Surgeon General's Report on Nutrition and Health (U.S. Department of Health and Human Services, 1988), and Trock et al. (1990). Most of these reviews have focused on data collected prior to 1988. In general, aggregate data have been equivocal in terms of a protective effect of dietary fiber against cancer. This review, therefore, focuses primarily on papers which have appeared since 1987 relating to fiber intake, colon cancer, and other cancers (Appendix Table).

A. HUMAN STUDIES

1. Colon cancer

There have now been several publications in which the findings of ecological and case-control studies have been summarized. It is important to note that the available data are the same but interpretations of reviewers may vary. For instance, Trock et al. (1990) found that the results of Pickle et al. (1984) can be listed under "equivocal support for protective effect of fiber;" whereas, other reviewers (Byers, 1988; Jacobs, 1988) concluded that Pickle's work provided no association between dietary fiber and colon cancer risk. The review by Trock et al. (1990b) went beyond the usual "yes" or "no" ratings and listed data as strongly supporting the protective effect of fiber, moderately supporting it, equivocally supporting it, or not supporting it. As such, these interpretations go beyond the original authors' conclusions.

The LSRO (Pilch, 1987) reviewed data from 18 ecological and 22 case-control studies. The report found fiber to be protective in 66.7 percent of the ecological studies and 36.4 percent of the case-control studies; 27.8 percent of the ecological studies and 40.9 percent of the case-control studies reported no effect; and enhancement was reported in 5.6 percent of the ecological studies and 22.7 percent of the case-control studies. Jacobs (1988) reviewed data pertaining to 24 ecological and 27 case-control studies and generally found protective effects in about half of them and no effect in 40 percent; Bingham (1990) classified the findings from 30 case-control studies conducted between 1969 and 1989 into outcomes relating to fiber, vegetables, cereals, and starch. Protective and non-protective effects (percent) were: fiber 50 and 41; vegetables 63 and 32; cereals 23 and 54; and starch 50 and 50. The results cited above are summarized in Table 1.
Table 1

Association between fiber intake and risk of colorectal cancer*

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ecological Studies</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>24</td>
<td>18</td>
<td>--</td>
</tr>
<tr>
<td>Protective (%)</td>
<td>54.2</td>
<td>66.7</td>
<td>--</td>
</tr>
<tr>
<td>No effect (%)</td>
<td>41.6</td>
<td>27.8</td>
<td>--</td>
</tr>
<tr>
<td>Enhancing (%)</td>
<td>4.2</td>
<td>5.6</td>
<td>--</td>
</tr>
<tr>
<td><strong>Case-control</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>27</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Protective (%)</td>
<td>44.4</td>
<td>36.4</td>
<td>50.0</td>
</tr>
<tr>
<td>No effect (%)</td>
<td>40.7</td>
<td>40.9</td>
<td>40.9</td>
</tr>
<tr>
<td>Enhancing (%)</td>
<td>14.8</td>
<td>22.7</td>
<td>9.1</td>
</tr>
</tbody>
</table>

* The numbers reflect studies with several reported outcomes, thus some studies reported separately on total fiber, cereals, etc. There is overlap in the studies reviewed.

It is evident that in the ecological studies there is a bias in favor of a protective effect of fiber; whereas in the case-control studies, findings of effectiveness and non-effectiveness are about equally distributed. In a very thorough review of diet and cancer published in 1988, Rogers and Longnecker stated: "Most epidemiologic studies of fiber or fiber-containing food intake in relation to risk of colorectal cancer are consistent with a very small inverse association or no association."

Thus ecological studies in which populations are compared yield a better correlation than do more precise (but much smaller) case-control studies. Another point to consider is that the current diet of patients with diagnosed colon cancer may be quite different from that ingested before diagnosis. Thus the ecological studies offer diet-disease data on entire populations while case-control studies may report on diets that were dictated by health status and therefore were not typical of prediagnosis food habits.

Graham et al. (1988) reviewed 428 confirmed cases of colon cancer in upstate New York counties and an equal number of controls. There were 225 males and 223 females. When risk was assessed with increasing fat, calories or Quetelet index, there was a significant trend toward increased risk. The *p* values for trend with fiber alone were 0.97 for men and 0.86 for women. An association with fiber was found only upon a logistic analysis of fiber in conjunction with other nutrients. They found a high fat-low fiber diet carried twice the risk of a low fat-high fiber diet. Their summary states: "Dietary fiber was only equivocally associated with risk."

These investigators also studied rectal cancer in 277 case-control pairs of males and 145 case-control pairs of females in the same area in New York state (Freudenheim et al., 1990a). They found that dietary fiber from vegetables but not from grains was associated with reduced risk. These investigators also analyzed fiber sources as they related to risk in the populations studied for colon and rectal cancer (Freudenheim et al., 1990b; Graham et al., 1988). Using food tables of Paul and Southgate (1978) and Pennington (1976), the investigators analyzed fiber content and composition and concluded that fiber from grain (especially the insoluble fiber) was associated with decreased risk of colon cancer in both males and females and fruit/vegetable fiber was associated with decreased risk in males only. Risk of rectal cancer was negatively associated with intake of fruit/vegetable fiber. The
magnitude of negative association was larger after controlling for fat. These findings differ from those of Slattery et al. (1988) who did not find grains to be protective. Whether Slattery et al. controlled for fat intake was not specified.

Slattery et al. (1988) carried out assessment of dietary risk for colon cancer in Utah studying 231 cases and 391 controls. Crude fiber was associated with decreased risk of colon cancer in both males and females. Highest quartiles of intake of fruits/vegetables were also associated with decreased risk in probands of both sexes. Grain intake was not protective. In examining their data on fiber type, risk for "dietary fiber" was higher in the highest quartile of intake than in the two intermediate ones. This suggests the possibility that at highest levels of intake some other interacting dietary factor may be depleted.

In another Utah study (West et al., 1989) 231 colon cancer cases and 391 controls were interviewed. The authors found positive associations with body–mass index, dietary fat, and fiber. Decreased risk was also associated with intake of β-carotene and cruciferous vegetables. Heilbrun et al. (1989) examined diet and colorectal cancer in American Japanese men. Over a 16–year period they identified 102 men with colon cancer and 60 men with rectal cancer who were compared with 361 cancer–free control subjects. Findings of fiber effects were related to fat intake. Thus in men with low fat intake (less than 61 g/d), there was a negative association with dietary fiber intake (p = 0.042). No such association was observed if fat intake exceeded 61g/d (p = 0.237). They found no association between dietary fiber intake and rectal cancer.

Lee et al. (1989) studied colorectal cancer in Singapore Chinese (203 cases, 405 controls). They saw a protective effect for high intake of cruciferous vegetables and a predisposing effect for a high meat/vegetable ratio. These findings held up when analysis was applied to colon cancer alone. The following were protective for rectal cancer: high intakes of protein, fiber, β-carotene, and vegetables. Gerhardsson de Verdier et al. (1990) studied 352 cases of colon cancer, 217 of rectal cancer, and 512 controls. Test for trend of fiber intake with colon cancer was not significant (p = 0.32) but significance was observed for rectal cancer (p<0.05). High fiber intake was associated with reduced risk of colon cancer in men and of rectal cancer in both men and women.

Willett et al. (1990) reported on the relation of meat, fat, and fiber intake to colon cancer risk in a prospective study of 88,751 women. They found no significant changes in colon cancer risk associated with total fiber, fruit, vegetable, or cereal fiber. Only fruit fiber showed a consistent trend for reduced risk with increasing intake, but the relationship was not statistically independent of meat intake. As noted for other studies the relative risk at the highest (fifth) quintile of total dietary fiber was 30 percent higher than that for the fourth quintile (0.90 vs 0.69). A positive association with fat was observed.

Recent studies do not clarify effects of fiber on colorectal cancer, but they are helpful for several reasons. They begin to show different effects for right and left colon, and they begin to focus on dietary interactions (Freudenheim et al., 1990a,b; Slattery et al., 1988). For example, the noncellulosic polysaccharides, containing mannose and galactose, appeared to protect against cancers in the ascending colons of men; galactose and uronic acid protected the descending colons of women (Slattery et al., 1988). Freudenheim et al. (1990b) reported some evidence that fruit and vegetable fiber seem to protect against cancer of the "distal bowel".

The data indicate no consistent relationship between risk and fiber, whether the fiber be total, crude, cereal, fruit, or grain. This might be corrected somewhat if fiber content were regarded in relation to other nutrients present in the food being analyzed. Animal studies have shown that caloric intake is a major determinant of susceptibility to chemically–induced or spontaneous cancers. Tannenbaum (1945) provided data on this point in the 1940s and recent reports bear it out (Kritchevsky and
Klurfeld, 1986). Lyon et al. (1987) have emphasized the importance of considering energy intake in assessing diet and colon cancer.

2. Breast cancer

Rose (1990) has reviewed the effects of fiber on incidence of breast cancer with emphasis on the influence of dietary fiber components or products, such as lignins, might exert on estrogen metabolism. He points out that vegetarians excrete more fecal estrogen than do omnivores and that the opposite is the case for urinary estrogens suggesting that excretion of estrogen via the colon may limit enterohepatic circulation.

Adlercreutz (1990) has also reviewed the data and reports that in a study in Boston (Adlercreutz et al., 1989), the pattern of high plasma estrogen levels, high urinary, and low fecal excretion of estrogen and low urinary excretion of lignans and phytoestrogens was seen in breast cancer cases. He attributes this pattern to a high intake of protein and fat and a concomitant low intake of fiber and grain products. However, in a Finnish study (Adlercreutz et al., 1987, 1988), excretion patterns were similar for cases and controls. Howe et al. (1990a) have published a combined analysis of 12 case–control studies of diet and breast cancer. This mode of data analysis provides a pool of 4427 cases, 434 population or neighborhood controls, and 1754 hospital controls. Relative risk rises significantly with total caloric intake or fat intake, and the most protective effect is seen with markers for vegetable or fruit intake, most notably vitamin C.

Using a different approach, Brisson et al. (1989) examined diet and breast cancer risk using mammographic features as the end point. Positive correlations were seen with total or saturated fat. Significant negative correlations were found with carotenoid and fiber intake.

There are three recently published case–control studies relating to diet and risk of breast cancer (see Appendix Table). Katsouyanni et al. (1988) studied 120 cases and an equal number of controls. They found no evidence for a positive effect of dietary fat or fiber but did find a significant protective effect of vitamin A. Pryor et al. (1989) studied 172 cases and 190 controls in an effort to relate adolescent diet to breast cancer in Utah. The cohort was aged 20–54 years. The authors commented on difficulties in recall of adolescent diets. In the premenopausal group there was a reduced risk of breast cancer between the highest quartile of intake and the other three for crude fiber, grains, and other sources of fiber. In the postmenopausal women risk rose markedly with increasing intake of crude fiber or "other" fiber but was slightly reduced for grains. The designation "grains" alluded to bread and cereal and other fiber relates to all other sources. Van 't Veer et al. (1990) studied 133 breast cancer cases and 238 population controls in the Netherlands. The energy–adjusted intake of dietary fiber in the cases (25.4 ± 6.7 g/d) was significantly lower than that of the controls (27.7 ± 7.4 g/d). The most striking correlation was with intake of cereal products.

3. Other cancers

a. Prostate cancer

Studies of diet and prostate cancer have not focused on fiber per se. Most studies have emphasized intakes of carotene or vitamin A, but these nutrients are often present in fiber–rich foods.

Wilson (1972) has postulated that elevated plasma androgen levels may lead to prostatic hyperplasia and eventually to cancer. Two studies of Seventh Day Adventist (SDA) and non–SDA men show that the vegans ingest more fiber and excrete more estrogen and testosterone (Pusateri et al., 1990; Ross
et al., 1990). This is similar to the argument Adlerkreutz (1990) presents for increased fecal steroid excretion being related to reduced breast cancer risk.

Oishi et al. (1988) studied 100 cases of prostatic cancer, 100 cases of benign prostatic hyperplasia and 100 hospital controls in Japan. Low intakes of beta carotene and vitamin A were correlated with the development of prostate cancer but intake of fiber was not. Severson et al. (1989) examined prospectively the incidence of prostate cancer in 7999 Japanese men followed for 18–21 years. They found 174 cases of prostate cancer. Intakes of rice and tofu were associated with decreased risk and seaweed with increased risk. Le Marchand et al. (1991) have reported on 452 cases of prostate cancer and 899 controls among the multiethnic population of Hawaii. Earlier studies (Kolonel et al., 1987, 1988) had suggested that increased risk was associated with increased vitamin A or beta-carotene intake in elderly men. In the new study the beta-carotene association is confined to level of intake of papaya (Le Marchand et al., 1991).

b. Miscellaneous cancers

Howe et al. (1990b) studied 249 cases of pancreatic cancer and 505 controls in Canada. Inverse correlations were found for fiber from fruit, vegetables, or cereal. A strong positive correlation was found with total caloric intake. Another Canadian study (Ghadirian et al., 1991) was carried out among French speaking citizens of Montreal whereas the study of Howe et al. (1990b) was done in Toronto. Examination of 179 cases and 239 controls indicated that the highest positive correlation was found with energy intake. Risk reduction was seen for increasing intake of fiber and beta-carotene, but the trends were not significant.

A study of 1244 cases of esophageal and gastric cancers and 1314 controls in north central China suggested increased risk with increased intake of wheat and corn and no elevation of risk connected with decreased intake of fresh fruit or vegetables (Li et al., 1989). The authors suggested a genetic component of cancer susceptibility was present in the population.

Lung cancer in Chinese women in Hong Kong was studied by Koo (1988). The probands had never smoked so that was not a confounding factor. Higher consumption of leafy green vegetables, carrots, tofu, fresh fish, and fresh fruit appeared protective.

4. Conclusion

Except for colon cancer, interest in fiber effects on cancer risks has been minimal. The foregoing studies suggest some influences of fiber on breast cancer; there is a report of inverse correlation between fiber intake and pancreatic cancer (Howe et al., 1990b); and there seems to be no link between fiber and risk of prostate cancer.

B. ANIMAL AND BIOMEDICAL STUDIES

1. Animal studies

While there has been a plethora of studies in animals, the results are difficult to interpret with regard to human effects. These problems in assessing results of animal experiments relating to fiber and colon cancer have been pointed out (Kritchevsky, 1983). Studies are carried out in rats of different strains; they are given different carcinogens or the same carcinogen by different routes of
administration; and the diets range from commercial to semipurified. In general, however, the only fiber which has been relatively consistent in its protective effect is wheat bran. Wheat bran leads to a consistent reduction in incidence of experimentally induced colon cancer. For example, Cohen et al. (1991) have shown that wheat bran (10 percent) will reduce incidence of N-nitrosomethyurea–induced mammary tumors by 27 percent when added to a high– (23.5 percent) fat diet and by 25 percent when added to a low– (5 percent) fat diet. The high–fat diet is 43 percent more carcinogenic than the low–fat diet. This is the first report of the efficacy of dietary fiber in an animal model for mammary cancer. The results of another study (Klurfeld et al., 1991) confirmed a fairly large body of data indicating that wheat bran is protective against 1,2–dimethylhydrazine–induced colon tumors compared with cellulose and showed that the combination of wheat bran with caloric restriction is more protective than wheat bran in an ad–libitum diet.

2. **Biomedical studies of markers of colon cancer risk**

Studies of the effects of dietary fiber on human fecal bile acid excretion were reviewed in the LSRO report (Pilch, 1987). There are a few recent studies relating to metabolic or other markers associated with increased risk of colon cancer. Hoff et al. (1986) carried out a double-blind study in which endoscopic screening for polyps was combined with a dietary survey. They found a relationship between polyp presence or polyp size and estimated total dietary fiber in men (β = 0.06). Intake of cruciferous vegetables was negatively correlated with polyp number and extent of dysplasia in adenomas. Allinger et al. (1989) reported that a shift from low– to high–fiber intake reduced total concentrations of soluble fecal fatty acids and deoxycholic acid, both of which may have risk factor significance. In another study, the diets of subjects with familial polyposis were supplemented with 13.5 g/d of wheat bran for 8 wk with the result that the thymidine–labeling index of biopsied mucosal cells was reduced significantly (Alberts et al., 1990).

Using enzyme activity as a marker of cell proliferation, Calvert and Reicks (1988) studied the thymidine kinase specific activity of colonic mucosa of rats fed various fibers for 4 weeks. A diet containing 5 percent guar gum lowered the index by 17 percent, and one containing 10 percent wheat bran reduced it by 33 percent. When the diet contained 5 percent carrageenan, the index was increased 3.8–fold.

C. **DISCUSSION**

1. **Dietary interactions**

High–fiber foods contain an array of the carbohydrate polymers which are included in the term "fiber," as well as a number of other macro– and micronutrients, all of which may possess important biological properties. An important aspect of diets containing high levels of fiber–containing foods is the displacement of other foods. As a consequence, certain nutrition–related effects may result from what has been displaced, or there may be combined effects of fiber and fiber–displaced nutrients. It is difficult to separate fiber effects from those of other active substances in foods, such as β–carotene which is found in vegetables. There are a few studies in which analysis of the fiber has been carried out, but results are not consistent. For example, the work of Heilbrun et al. (1989) and Lee et al. (1989) suggests interaction between the fiber component of the diet and other factors which have not been identified. Slattery et al. (1988) found that in males and females in Utah, the odds ratio (OR) for risk of colon cancer at the highest quartile of starch intake was greater than at the third quartile. Grain intake provided a similar picture for Utah females. These findings suggest an optimum level
for some foods which, when exceeded, may increase rather than decrease risk of colon cancer. Similar data on other cancers are lacking.

2. **Summary of certain associated factors in the cancer–fiber relationship**

   a. **Basis of association between dietary fiber and cancer**

   The ingredient, dietary fiber is a food component or may be added to foods. Whether the observed effects are due strictly to the fiber or to other components of the fiber–rich food or to a combination of these remains to be determined.

   b. **Level of intake for a beneficial effect**

   There is no agreed-upon measure as to the level of intake at which beneficial effects related to cancer are observed. The supporting data are far from unanimous. Furthermore, whether the effects of fiber are due to the fiber per se, accompanying substances, or displacement of fat and/or calories from the diet by fiber has not been established with certainty.

   c. **Optimal level of consumption and duration of effect**

   There are suggestions as to optimum level of intake for "better health" (e.g., normal bowel function) but not for prevention of disease. The FASEB review (Pilch, 1987) suggested that dietary fiber intake be linked to caloric intake and proposed an intake of 10–13g/1000 kcal. There are no data relating to transience of a fiber effect although this is amenable to experimental testing.

   d. **Applicability to total U.S. population**

   Generalization of available scientific information to the entire U.S. population is difficult because data to support strongly the concept that fiber is protective are insufficient and there were few reports on subjects below 25 and over 65 years old. Presumably persons at high risk such as those with a family history of cancer would benefit most. Further, it is not clear as to whether the protective effects observed in some studies are the result of the fact that most high–fiber diets are low–fat diets. In addition, accumulating evidence suggests that caloric intake is a strong risk factor. For example, Lyon et al. (1987) concluded: "Total energy intake must be evaluated before attempting to assign a causal role to any food or nutrient that may be postulated to play a role in colon cancer."
e. Significant food sources of dietary fiber

Significant dietary sources of fiber (general) are whole grains, legumes, fruits, vegetables and nuts. In addition, isolated fibers such as wheat and oat bran are added to various foodstuffs and prepared food products.

f. Influence of other dietary, nutritional, or health factors

In a marginally or undernourished population, high fiber intake may lead to trace mineral deficiency. This might also be the case in specific sections of our population (old people, children) (Pilch, 1987).

g. Safety concerns about reasonable or high levels of consumption

In general, reasonable consumption of a high-fiber diet poses no real health threat and may lead to less calorically dense diets. Sigmoid volvulus and persorption have been reported, but these are rare even in underdeveloped populations ingesting a high-fiber diet. Excessive consumption of fiber supplements is more likely to result in intestinal problems or poor absorption of trace minerals than would be expected from a high-fiber diet.

h. Difference in efficacy among food sources and supplements

Most of the cancer studies are based on retrospective dietary data and not on effects of isolated fibers. The only material which has been tested as fiber is wheat bran which in concentrated bulk is probably very little different from its native state. Although the bran, per se, may not differ from its native state, the total diet composition and associated nutritional effects may vary if bran is consumed as an additive to non-cereal foods compared with diet composition when bran is consumed in whole grain cereals. Wheat bran is a complex mixture which contains several types of fiber, some protein and fat, and trace minerals.

i. Critical gaps in knowledge

Questions which have not been answered satisfactorily are:

1) Is the putative beneficial effect a result of fiber or another component of the fiber-rich food such as β-carotene? That is, what are the contributions of fiber versus other plant components to lowering cancer risk?

2) If it is fiber, which one(s)? What are the relative contributions of specific categories of fiber types or fiber-rich foods to measurable beneficial effects?
3) Is it higher fiber or lower fat? To what extent can the putative protective effects of fiber be separated from the effects of reduced fat intake?

4) If fiber is shown to be actively protective, what should be the dosage to protect against various types of cancer?

3. Overall summary

Various beneficial effects have been suggested for foods rich in dietary fiber including reduction of blood cholesterol levels and the risk of developing coronary atherosclerosis. Whole foods high in fiber, high-fiber fractions such as wheat bran, concentrated fibers such as pectins or cellulose, and fiber-enriched foods are types of fiber containing products.

Interpretation of data is hampered by a number of factors such as the lack of a generally accepted definition of dietary fiber and limited knowledge of the physiological effects, mechanisms of action, and the effects of interactions with other dietary components of various types of dietary fiber. Moreover, simple, reliable methods for rapid and accurate qualitative and quantitative assessment of fiber in foods are not available. Consequently, the accuracy of most estimates of dietary fiber intakes is limited.

Major reviews of data collected prior to 1988 have generally shown the data for a possible effect of dietary fiber against cancer to be equivocal. Publications since 1987 that are evaluated in this report again showed no robust, consistent effect for protection against colorectal cancer; however, results of seven of nine cited studies associated decreased risk with increased intakes of dietary fiber. One study showed decreased risk when high-fiber was combined with low-fat, and one large, prospective, cohort study found no significant association between risk and intake of total fiber, fruits, vegetables, and cereals.

Three recent investigations examined biomedical markers of colon cancer risk. In one, a trend toward fewer and smaller colorectal polyps was observed with increasing total dietary fiber in subjects at high risk for colorectal cancer, and intake of cruciferous vegetables was negatively correlated with polyp number and degree of dysplasia in adenomas. Another study showed reduced concentrations of soluble fecal fatty acids and deoxycholic acid with high-fiber intakes, and a third study reported reduced thymidine labeling in biopsied colorectal mucosal cells in familial polyposis patients given a wheat bran supplement.

For breast cancer, three recent reviews are noteworthy. In relation to the circulating estrogen theory of the etiology of breast cancer, one review concluded that vegetarians (1) excrete more fecal estrogen, thus reducing enterohepatic circulation and (2) have a higher urinary excretion of lignans, a family of compounds formed in the intestine from fiber-associated precursors. A second review noted that breast cancer patients had high plasma estrogen levels, high urinary and low fecal excretion of estrogen, and low urinary excretion of lignans and phytoestrogens, all associated with high intakes of proteins and fat and low intakes of fiber-rich foods and grain products. A third review was a meta-analysis of 12 case-control studies of diet and breast cancer which suggested a protective effect of vegetables, fruit, and vitamin C.

Three of four reports of recent investigations associated decreased risk with increased intakes of carotenoids and fiber, or with crude fiber and grains, or cereals. The fourth study found no association between fiber and risk of breast cancer. Decreased risk of prostatic cancer with
higher intakes of fiber was inferred from the circulating hormone hypothesis in one study and from higher intakes of rice and tofu in another study. In a third investigation, risk appeared to increase with high consumption of papaya, or, in a fourth study, with increased intake of β-carotene or vitamin A. A fifth study found no association between fiber and prostate cancer.

Decreased risk of pancreatic cancer was associated with increased intakes of fruit, vegetables, and cereal in one study; in another, a nonsignificant trend toward decreased risk with higher intakes of fiber and β-carotene was reported. Results of a large case-control study of esophageal and stomach cancer in China suggested an increased risk with higher intakes of wheat and corn but no increased risk with low intakes of fresh fruit and vegetables. Risk of lung cancer in nonsmoking women in Hong Kong was inversely associated with consumption of leafy green vegetables, carrots, tofu, and fresh fruit.

In animal studies, the only fiber source which has been relatively consistent in its protective effect against chemically induced colon tumors is wheat bran. One recent study shows it to protect against mammary tumors as well. In addition, diets containing guar gum or wheat bran lowered the thymidine kinase specific activity of rat colonic mucosa by 17 percent and 33 percent respectively compared with controls.

The Surgeon General's Report (U.S. Department of Health and Human Services, 1988) stated, "While inconclusive, some evidence suggests that an overall increase in intake of foods high in fiber might decrease risk for colon cancer," and "Limited information is available on the types of dietary fiber that might protect against cancer. Research will have to define the importance of various fiber compounds relative to risk for specific cancers."

The National Research Council (1989) report states, "Diets high in plant food--i.e., fruits, vegetables, legumes, and whole grain cereals--are associated with a lower occurrence of coronary heart disease and cancer of the lung, colon, esophagus, and stomach," and, "Epidemiologic and clinical studies indicate that a diet characterized by high-fiber foods may be associated with a lower risk of CHD, colon cancer, diabetes mellitus, diverticulosis, hypertension, or gallstone formation, but there is no conclusive evidence that it is dietary fiber, rather than the other components of vegetables, fruit, and cereal products, that reduces the risk of those diseases," and, "In general, the evidence for a protective role of dietary fiber per se in CHD, colon and rectal cancers, stomach cancer, female gynecologic cancers, diabetes, diverticulosis, hypertension and gallstones is inconclusive."

The present review of the recent literature leads to similar conclusions. Resolutions of the weight of scientific evidence will require separation of dietary fiber–cancer relationships and differentiation of specific fiber effects from those attributable to the whole food. Until this is done, the weight of scientific evidence must be viewed as inconclusive.

D. GENERAL CONCLUSIONS

The Surgeon General's Report, "Nutrition and Health" (1988) concluded that high-fiber diets are associated with lower rates of some types of cancer. The conclusion is non-specific and the data from studies noted in the appendix table of the present report are far from unanimous on this point. The NRC report, "Diet and Health" (1989), echoes the earlier NRC report (1982) which noted that findings were provocative, but insufficient to be conclusive. A critical review of the recent scientific literature leads to a similar conclusion. The subject is a very complex nutritional problem. Resolution of the issues involved will require separation of dietary fiber–cancer relationships and differentiation of specific fiber effects from the general ones attributable to the whole food (fiber, macronutrients,
vitamins, minerals, total energy, etc.). Until this is done, the weight of scientific evidence must be viewed as inconclusive.
III. BIBLIOGRAPHY*


* This bibliography contains all reference citations that are either in the text or the appendix table or both.


APPENDIX

CRITERIA FOR INCLUSION OF ARTICLES IN APPENDIX TABLE

Articles in peer-reviewed journals related to the topic of this review were selected primarily on the basis of date and content. In general, papers appearing in 1987 or thereafter were included, provided that they presented original data from studies in humans. Certain items tabulated for the sake of completeness may not have been cited in the body of the text if their weight or relevance did not add significantly to development of the author's argument. Reviews have not been listed except as they included new data or useful meta-analyses.
## APPENDIX TABLE. INFLUENCE OF DIETARY FIBER ON CANCER

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number &amp; Description of Subjects</th>
<th>Duration</th>
<th>Source &amp; Identity of Test Material</th>
<th>Dosage</th>
<th>Base Diet</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Colorectal</td>
<td>Prospectively clinical trial of dietary fiber on markers of colorectal cancer</td>
<td>17 pts, 54-70 yr, at high risk of recurrent colorectal cancer</td>
<td>8 wk</td>
<td>All Bran wheat bran supplement</td>
<td>13.5g/d</td>
<td>Usual diet</td>
<td>Pilot study, small N, NR, short-term</td>
<td>Overall 22% lower in DNA synthesis &amp; cellular proliferation after 2 mo of wheat bran supplementation</td>
<td>Results appear to confirm a mechanism of action of wheat bran fiber.</td>
</tr>
<tr>
<td>Allinger et al., 1989</td>
<td>Dietary intervention study of effect on colorectal cancer diet on fecal bile acids and deoxycholate</td>
<td>28 volunteers (6 male, 20 female) 26-61 yrs</td>
<td>3 mo</td>
<td>Increased intake of fruit and vegetables</td>
<td>DF estimated at 30g/d</td>
<td>Usual mixed diet before experiment</td>
<td>Uncertainty about biologic mechanisms of DF</td>
<td>Lower concentration of soluble fatty acids and deoxycholic acid in fecal water</td>
<td>Useful contribution; source of test hypotheses</td>
</tr>
<tr>
<td>DeCosse et al., 1989</td>
<td>FBCT of wheat fiber, and vitamins C and E on number and size of colorectal polyps</td>
<td>62 pts with familial adenomatous polyposis who had colectomies and ileo-colonic anastomoses</td>
<td>4 yr</td>
<td>Commercial bran cereal</td>
<td>High-fiber: 22.5g/d plus 400 mg α-tocopherol and 4 g ascorbic acid/d</td>
<td>Usual diet</td>
<td>Fiber consumption showed downward trend with time, but greater intake prevailed in high-fiber group. Study population was ambulatory.</td>
<td>58 pts assessable in study. Benign large bowel neoplasia was inhibited by grain fiber supplements &gt;11g/d; however, the effect was limited. Prescribed high-fiber supplement seemed to lower polyp size and number.</td>
<td>Useful results in a unique difficult-to-acquire and administer study population. It is not clear whether changes in colorectal cell proliferation reflect similar changes in colon.</td>
</tr>
<tr>
<td>Freudenheim et al., 1990a</td>
<td>Retrospective CC study</td>
<td>Rectal cancer: cases: 277 male, 145 female controls: 277 male, 145 female</td>
<td>1978 to 1986</td>
<td>Vegetables, cereals, and grains</td>
<td>Low to high: by quartiles ( \delta ) by tertiles</td>
<td>Usual diet</td>
<td>Some unavoidable error in dietary intake estimates; many CC studies had few cases of colorectal cancer.</td>
<td>Increased intakes of vitamin C, carotenoids, and vegetable fiber were protective</td>
<td>High quality study</td>
</tr>
<tr>
<td>Freudenheim et al., 1990b</td>
<td>Reassessment of results of Graham et al. (1988) and Freudenheim et al. (1990a)</td>
<td>Vegetables, cereals, grains</td>
<td>1975 to 1986</td>
<td>Low to high</td>
<td>Usual diet</td>
<td>Colon: ( \delta ) - grain fiber ( \delta ) - decreased risk; ( \delta ) - grain fiber ( \delta ) - decreased risk</td>
<td>A reassessment of earlier data. Sex differences exist.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

1 The references cited in this table refer either to the text, this table, or both.
### APPENDIX TABLE. INFLUENCE OF DIETARY FIBER ON CANCER

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number &amp; Description of Subjects</th>
<th>Duration</th>
<th>Source &amp; Identity of Test Material</th>
<th>Dosage</th>
<th>Base Diet</th>
<th>Other Factors Affecting Date Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Friedman et al., 1988</td>
<td>In-vitro study of effect of fiber on deoxycholic acid (DGA)-induced lysis of cultured colonic epithelial cells</td>
<td>Colonic epithelial cells from 18♂ and 13♀ at high risk of colon cancer</td>
<td>Purified peyrium fiber</td>
<td>Amount not specified</td>
<td></td>
<td></td>
<td></td>
<td>Increase in percentage of surviving colonies at 10 nM, 0.1nM, 0.5 nM, and 1.0 mM were 6.1, 4.1, 3.8, and 0.8. Propionate was potent colonocyte mitogen.</td>
<td>Relevance to in vivo effects not clear</td>
</tr>
<tr>
<td>Gerhardsen de Verdier, 1990</td>
<td>Population-based case-referent study of diet, body mass, and colorectal cancer.</td>
<td>729♂ and 9♀ cancer pts (452 colon, 266 rectum) 624 controls</td>
<td>January 1988 - March 1989</td>
<td>Food-frequency questionnaire and analysis for fiber</td>
<td>Low to high by quintiles</td>
<td>Usual diet during 6 yr before cancer dx</td>
<td>Dietary recall up to 6 yr in the past limits accuracy of intake estimates</td>
<td>High fiber intake associated with decreased risk of colon cancer in♂ and rectal cancer in♂ and ♀. RR = 0.6, 1.2 for colon RR = 0.5, 0.4 for rectum</td>
<td>A carefully conducted study</td>
</tr>
<tr>
<td>Graham et al., 1989</td>
<td>Retrospective CC study</td>
<td>Colon cancer population: cases: 205♂, 223♀ controls: 205♂, 223♀</td>
<td>1975-1984</td>
<td>Vegetables, cereals, and grains Food-frequency interviews</td>
<td>Low to high by quartiles</td>
<td>Usual diet</td>
<td>Some unavoidable error in dietary intake estimate despite great care in food-frequency interviews</td>
<td>Dietary fiber only equivocally associated with colon cancer risk. Seems to reduce risk for ♀. (For added information see Freudenheim et al., 1990b.)</td>
<td>Carefully conducted study</td>
</tr>
<tr>
<td>Hellbrun et al., 1989</td>
<td>Cohort and CC study</td>
<td>Cohort = 8006 American Japanese ♂ Cancer cases during &gt;10 yr follow-up: 102 colon, 60 rectal. Cancer-free control: 361♂</td>
<td>1965-1985</td>
<td>Vegetables, cereals, grains from usual diet</td>
<td>Cancer cases: 11.5-12.1 g/d Controls: 11.6 g/d</td>
<td>Usual diet</td>
<td>Only one 24-hr dietary-recall interview to estimate fiber and nutrient intake</td>
<td>When fat intake &lt; 61 g/d, colon cancer risk drops as fiber increases - p = 0.045. No significant association between fiber intake and risk of rectal cancer</td>
<td>Preliminary results</td>
</tr>
<tr>
<td>Lee et al., 1989</td>
<td>Hospital-based CC study of colorectal cancer</td>
<td>Singapore Chinese Cases: Colon = 77♂, 55♀ Rectum = 44♂, 27♀ Controls: 239♂, 197♀</td>
<td>1985-1987</td>
<td>Vegetables</td>
<td>Low to high by tertiles of intake</td>
<td>Usual diet</td>
<td>Uncertainties of actual dietary intakes</td>
<td>Cruciferous vegetables protect against colon and rectal cancer. High meat to vegetable ratio increases risk of colon cancer; no consistent trend for fat and fiber.</td>
<td>Apparent lack of fat and fiber influence needs further study.</td>
</tr>
<tr>
<td>Reddy et al., 1989</td>
<td>Prospective dietary intervention trial in healthy volunteers to determine effects of different DFs on fecal mutagens, acid and neutral sterols. Randomized, crossover design, each subject tasted for 5 wk on each of 3 DF supplements</td>
<td>19 healthy volunteers who exhibited high levels of fecal mutagens</td>
<td>7 mo (Approximately)</td>
<td>Wheat bran, oat fiber, cellulose</td>
<td>10 g/d as dietary supplement Normal diets in control periods</td>
<td>Self-selected, high-fat, low-fiber</td>
<td>Effects on fecal secondary bile acids and mutagenicity: wheat bran - decrease cellulose - decrease oat fiber - no effect</td>
<td>Effects on fecal secondary bile acids and mutagenicity: wheat bran - decrease cellulose - decrease oat fiber - no effect</td>
<td>Type of fiber appears important in determining effects.</td>
</tr>
</tbody>
</table>
## APPENDIX TABLE. INFLUENCE OF DIETARY FIBER ON CANCER

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number &amp; Description of Subjects</th>
<th>Duration</th>
<th>Source &amp; Identity of Test Material</th>
<th>Dosage</th>
<th>Base Diet</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rosen et al, 1989</td>
<td>Swedish correlational study of colon cancer mortality and food acquisition for households in different regions</td>
<td>NA</td>
<td></td>
<td>Fiber calculated from food expenditure</td>
<td>Usual diet</td>
<td></td>
<td>Gross uncertainties of actual dietary intakes; time mismatch between survey of food purchases and mortality data</td>
<td>Inverse relationship between consumption of dietary fiber, crisp bread and colon cancer mortality in $&lt; \frac{1}{2}$ and $\geq \frac{1}{2} r=0.62$</td>
<td>Data suggest protective effect of dietary fiber but statistical power is weak.</td>
</tr>
<tr>
<td>Slattery et al, 1988</td>
<td>Population-based CC study of dietary fiber in relation to colon cancer</td>
<td>Cases: 112 $\sigma$, 119 $\varphi$ Controls: 185 $\sigma$, 206 $\varphi$</td>
<td>1970-1983</td>
<td>Dietary fruits, vegetables, grains, estimated by food-frequency questionnaire</td>
<td>Low to high by quartiles</td>
<td>Usual diet</td>
<td>Small N to support the various parameters analyzed; uncertainty of dietary intake</td>
<td>$&lt; \frac{1}{2}$ and $\geq \frac{1}{2}$ intake of fruits, veg inversely related to colon cancer risk. Grains not protective. DF and NDF: no consistent relationship; mannose, galactose protective in ascending colon in $&lt; \frac{1}{2}$, galactose and uronic acid protective in ascending colon in $\geq \frac{1}{2}$</td>
<td>Useful study</td>
</tr>
<tr>
<td>Slattery et al, 1989</td>
<td>Correlation analysis of 2 population-based CC studies. Dietary Intakes were estimated 2-5 yr before cancer dx.</td>
<td>411 colon cancer pts</td>
<td>Cancers dx 1970-1971</td>
<td>Dietary fiber</td>
<td>Low to high by quartiles</td>
<td>Usual diet, precancer dx</td>
<td>Dietary recall 2-5 yr in the past limits accuracy of intake estimates</td>
<td>Highest quartile of fiber intake associated with decreased survival compared with lowest quartile of intake</td>
<td>Limited statistical power</td>
</tr>
<tr>
<td>Trock et al, 1990</td>
<td>Review and appraisal of all epidemiological studies of colorectal cancer and fiber, veg, grains, or fruit published from 1970 through 1988 Meta analysis of 16 CC studies Total covered: 57 observational and 23 CC</td>
<td>N/A</td>
<td>Span of studies about 18 yr</td>
<td>Fiber from all fiber-containing foods</td>
<td>High and low levels of consumption</td>
<td>Usual diets</td>
<td>A majority of studies showed protective effect associated with fiber-rich foods. When highest and lowest quintile of intake were compared the estimated combined ORs were: 0.57 for fiber-rich diets 0.48 for vegetable consumption.</td>
<td>A useful analysis</td>
<td></td>
</tr>
<tr>
<td>West et al, 1989</td>
<td>CC study of diet and colon cancer</td>
<td>Cases: 112 $\sigma$, 119 $\varphi$ Controls: 185 $\sigma$, 206 $\varphi$</td>
<td>1970-1983</td>
<td>Dietary fruits, vegetables, estimated on food-frequency questionnaire and analysis for crude fiber, NDF, and sugar fractions</td>
<td>Low to high by quartiles</td>
<td>Usual diet 1-2 yr before cancer dx</td>
<td>Dietary recall limits accuracy of intake estimates</td>
<td>Fiber (crude fiber) was protective in $&lt; \frac{1}{2}$ (OR = 0.5). $&lt; \frac{1}{2}$ risk estimates for fibers = 0.3 and cruciferous vegetables = 0.3</td>
<td>Data support the fiber hypothesis</td>
</tr>
<tr>
<td>Willett et al, 1990</td>
<td>Prospective cohort study of relationships between intakes of meat, fat, and fiber and colon cancer</td>
<td>Cohort 88,751 $\sigma$, 34-59 yr By 1988, incident cases of colon cancer = 150</td>
<td>1980-1986</td>
<td>Dietary questionnaire and estimation of fiber content</td>
<td>Low to high by quintiles</td>
<td>Usual diet, precancer dx</td>
<td>Dietary recall limits accuracy of intake estimates</td>
<td>Low intake of fiber from fruits was associated with increased risk of colon cancer, but not statistically independent of meat intake.</td>
<td>A carefully conducted study</td>
</tr>
<tr>
<td>Reference</td>
<td>Study Design</td>
<td>Number and Description of Subjects</td>
<td>Duration of Study</td>
<td>Source and Identity of Test Material</td>
<td>Dosage of Test Material</td>
<td>Base Diet</td>
<td>Other Factors Affecting Data Interpretation</td>
<td>Results</td>
<td>Assessment of Study</td>
</tr>
<tr>
<td>-----------</td>
<td>--------------</td>
<td>------------------------------------</td>
<td>------------------</td>
<td>--------------------------------------</td>
<td>------------------------</td>
<td>----------</td>
<td>------------------------------------------</td>
<td>---------</td>
<td>---------------------</td>
</tr>
<tr>
<td>B. Breast Katsouyanni et al., 1988</td>
<td>CC study of diet and breast cancer</td>
<td>120 cases controls: 120 non-cancer pts</td>
<td>1983-1984</td>
<td>Dietary intake estimates from food frequency questionnaire</td>
<td>ND</td>
<td>Usual pre-cancer dx diet</td>
<td>Uncertainty of actual dietary intakes</td>
<td>No evidence of a protective effect of dietary fiber, but Vitamin A protective No 1 risk from dietary fat</td>
<td>Apparent lack of fiber effect needs validation.</td>
</tr>
<tr>
<td>Pryor et al., 1989</td>
<td>Population-based CC study of adolescent diet and breast cancer.</td>
<td>172 cases 190 controls 20-54 yr</td>
<td>1960-1983</td>
<td>Dietary intakes estimates from food-frequency interviews</td>
<td>ND</td>
<td>Adolescent diet as estimated by diet interview</td>
<td>Possible biased estimate from low response rate, recall bias, and lack of precision in dietary instrument</td>
<td>Postmenopause: high-fiber intake related to 1 ORs, but grain fiber related to 1 risk in pre- and postmenopause subjects</td>
<td>Level of risk unclear, nutrient source may be important.</td>
</tr>
<tr>
<td>Rohan et al., 1988</td>
<td>Population-based CC study of diet and breast cancer</td>
<td>Cases: 461; 20-74 yr Controls: 461 no bx breast cancer, age-matched</td>
<td>1982-1984</td>
<td>Dietary intakes estimated from self-administered food-frequency questionnaire and food composition tables</td>
<td>ND</td>
<td>Usual pre-dx diet</td>
<td>Uncertainty of actual dietary intakes. Dietary energy, protein, fat, carbohydrate (including fiber), and vitamin A were study foci.</td>
<td>Risk decreased nonuniformly at upper 3 quintiles of fiber intake; statistically nonsignificant</td>
<td>Extensive study that suggests a protective effect of fiber</td>
</tr>
<tr>
<td>Van't Veer et al., 1990</td>
<td>Population-based CC study of dietary fiber, β-carotene, and breast cancer</td>
<td>133 cases, 25-44 yr 238 controls, 65-84 yr</td>
<td>1985-1987</td>
<td>Dietary intakes estimated from dietary history interviews</td>
<td>ND</td>
<td>Usual diet during 12 mo preceding dx</td>
<td>Uncertainty of actual dietary intakes</td>
<td>Fiber intake lower in cases than controls. Beta-carotene similar in both groups. OR for highest quartile intake of cereal products: 0.42; OR for fiber intake = 0.55, but trend NS</td>
<td>Results suggest a diet rich in vegetable products may lower risk of breast cancer.</td>
</tr>
</tbody>
</table>
### APPENDIX TABLE: INFLUENCE OF DIETARY FIBER ON CANCER

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number and Description of Subjects</th>
<th>Duration of Study</th>
<th>Source and Identity of Test Material</th>
<th>Dosage of Test Material</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>C. Pancreas Gladirian et al., 1991</td>
<td>Population-based CC study of diet and pancreatic cancer in French-speaking Canadians</td>
<td>Cases: 179 (97 ♂, 82 ♀); Controls: 239, age- and sex-matched</td>
<td>1984–86</td>
<td>Dietary intakes estimated from interviewer-administered food-frequency questionnaire; Fiber estimated as total and crude</td>
<td>ND</td>
<td>1- and 10-yr pre-dx diet estimate; Uncertainty of actual dietary intakes despite extra care in administering food-frequency questionnaire</td>
<td>No significant effect of estimated fiber intake on risk</td>
<td>Fiber was not a primary study focus.</td>
</tr>
<tr>
<td>Howe et al., 1990b</td>
<td>Population-based CC study of diet and pancreatic cancer</td>
<td>Cases: 249 (141 ♂, 108 ♀); Controls: 509, age- and sex-matched</td>
<td>1983–1986</td>
<td>Total fiber from fruit, veg., and cereals; Dietary intakes estimated from interviewer-administered food-frequency questionnaire; Fiber estimated from food tables</td>
<td>ND</td>
<td>Usual diet 1-2 yr before interview; Uncertainties related to actual dietary intakes and validity of information from proxies</td>
<td>Fiber – highest quartile of intake RR = 0.42 p&lt;0.0004 Positive association with total caloric intake</td>
<td>Study carefully conducted; supports the need for added investigation</td>
</tr>
<tr>
<td>D. Prostate Le Marchand et al., 1991</td>
<td>Further analysis of a 1987 CC study of vitamin A and prostate cancer (Folonier et al., 1987)</td>
<td>Cases: 452 multi-ethnic ♂</td>
<td>1977–1983</td>
<td>Quantitative bx of food frequency and portions size</td>
<td>Usual pre-dx diet</td>
<td>Limitations in dietary data</td>
<td>No association of yellow-orange fruits and veg., tomatoes, dark green veg., and cruciferous veg., with risk of prostate cancer except in ♂ &gt; 70.9 yr; papaya increased OR to 2.8 p&lt;0.0001</td>
<td>Useful study leading to test hypotheses</td>
</tr>
<tr>
<td>Oishi et al., 1988</td>
<td>CC study of prostatic cancer and diet</td>
<td>Cases: 100, 50–79 yr; Age-matched controls: 100 BPH, 100 hospital pts with no prostate pathology</td>
<td>1981–1984</td>
<td>Food consumption and portion size interview</td>
<td>Usual diet 6 yr before interview</td>
<td>Limitation in accuracy of dietary intake estimates</td>
<td>Estimated fiber intake was not correlated with risk of prostate cancer.</td>
<td>Fiber was 1 of 7 dietary component categories analyzed.</td>
</tr>
</tbody>
</table>
## APPENDIX TABLE. INFLUENCE OF DIETARY FIBER ON CANCER

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study Design</th>
<th>Number and Description of Subjects</th>
<th>Duration of Study</th>
<th>Source and Identity of Test Material</th>
<th>Dosage of Test Material</th>
<th>Other Factors Affecting Data Interpretation</th>
<th>Results</th>
<th>Assessment of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severson et al., 1989</td>
<td>Prospective cohort study of demographics, diet, and prostate cancer</td>
<td>7999 Japanese-American ♂️; Incident cases: 74</td>
<td>1965-1986</td>
<td>Food-frequency questionnaire plus 24-hr diet recall at interview</td>
<td>ND</td>
<td>Limitation in dietary data; 23 foods or food-component categories analyzed</td>
<td>RR: tofu 0.35, fruit 1.31, seaweed 1.74, rice 0.38</td>
<td>More research needed to sort out diet-prostate cancer relationships</td>
</tr>
<tr>
<td>E. Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Koo, 1988</td>
<td>Retrospective CC study of diet and lung cancer in non-smoking Hong Kong Chinese women</td>
<td>Cases: 88 ♂️, mean age 57.8 yr District-matched controls: 137 All subjects never smoked tobacco</td>
<td>1981-1993</td>
<td>Dietary interview of food consumption patterns</td>
<td>Usually diet 1 yr before cancer dx</td>
<td>Limitations in dietary data and number of patients</td>
<td>Adjusted RR: 2.4 and 2.8 for lowest tertile of intake of fresh fruit and fresh fish, respectively. Protective effects of veg., carrots, tofu, fresh fruit, and fresh fish mostly applied to adenocarcinoma or large cell tumors. Only fresh fruit affected risk of squamous and small cell tumors.</td>
<td>Fruit may contain a protective factor other than fiber.</td>
</tr>
<tr>
<td>Li et al., 1989</td>
<td>Population-based CC study of diet, other risk factors, and cancers of esophagus, cardia, in Linxian, China</td>
<td>1244 cases (758 ♂️, 486 ♂️), 35-64 yr Age- and sex-matched controls (789 ♂️, 555 ♂️)</td>
<td>1984-1985</td>
<td>Interviewer administered food-frequency questionnaire</td>
<td>Usually diet in the late 1950s and the late 1970s</td>
<td>Limitations in dietary data</td>
<td>OR: wheat 2.0, corn 1.5, millet 0.7, fresh veg. 1.5, dried veg. 0.6, fruit 1.0</td>
<td>Slight increased risk for fiber-rich foods Cause of high incidence of esophageal cancer in Linxian was not identified.</td>
</tr>
</tbody>
</table>

### ABBREVIATIONS:

- BPH = benign prostatic hypertrophy
- CC = case control
- DF = dietary fiber
- dx = diagnosis
- FA = fatty acid
- hx = history
- N/A = not applicable
- ND = not described
- NDF = neutral detergent fiber
- NR = nonrandom
- NS = nonsignificant
- OR = odds ratio
- PRCT = prospective, randomized, controlled trial
- pt = patient
- RR = relative risk
- SC = self-controlled