Cereals, legumes, and chronic disease risk reduction: evidence from epidemiologic studies1–3

Lawrence H Kushi, Katie A Meyer, and David R Jacobs Jr

ABSTRACT There is growing evidence that cereals and legumes play important roles in the prevention of chronic diseases. Early epidemiologic studies of these associations focused on intake of dietary fiber rather than intake of grains or legumes. Generally, these studies indicated an inverse association between dietary fiber intake and risk of coronary artery disease; this observation has been replicated in recent cohort studies. Studies that focused on grain or cereal intake are fewer in number; these tend to support an inverse association between intake of whole grains and coronary artery disease. Studies on the association of dietary fiber with colon and other cancers have generally shown inverse relations, but whether these relations are attributable to cereals, other fiber sources, or other factors is less clear. Although legumes have been shown to lower blood cholesterol concentrations, epidemiologic studies are few and inconclusive regarding the association of legumes with risk of coronary artery disease. It has been hypothesized that legumes, in particular soybeans, reduce the risk of some cancers, but epidemiologic studies are equivocal in this regard. Overall, there is substantial epidemiologic evidence that dietary fiber and whole grains are associated with decreased risk of coronary artery disease and some cancers, whereas the role of legumes in these diseases appears promising but as yet inconclusive. Am J Clin Nutr 1999;70(suppl):451S–8S.

KEY WORDS Dietary fiber, whole grains, legumes, cereals, coronary artery disease, cardiovascular disease, cancer, chronic disease risk, chronic disease prevention

INTRODUCTION The observation that diets low in meat and high in cereals and legumes are beneficial for health has recently become a topic of scientific interest, but was noted at least as far back as the Old Testament. In the first chapter of the Book of Daniel (1), Daniel beseeched King Nebuchadnezzar’s prince of eunuchs not to feed him the king’s meat and wine, but to feed him a diet of pulses (cereals and legumes) instead. The prince of eunuchs, concerned that Daniel and his friends would look callow in comparison with others, feared the King would be displeased. To this, Daniel proposed that he and his friends be fed the pulse diet for 10 days, after which their countenance could be compared with that of others who were fed the king’s meat. In this earliest of recorded feeding experiments, it was observed after the intervention period that indeed, Daniel and his group appeared “fairer and fatter in flesh” than the others, and so they were provided the diet of pulses rather than the diet of meat. More recently, the role that cereals and legumes may play in the etiology of chronic diseases was highlighted by hypotheses put forth by Burkitt and Trowell (2), who suggested that dietary fiber may be beneficial for preventing several diseases that are common in Western societies. Based on observations of diet and disease in Africa compared with the United Kingdom and other industrialized nations, they proposed that the refining of grains and lack of dietary fiber may be important in diseases such as large bowel cancer (3), coronary artery disease (4), and diabetes (5, 6).

These observations stimulated substantial research into the association of dietary fiber intake with these diseases. Much of this research has focused on understanding the mechanisms by which dietary fibers may influence the etiology of these diseases. Thus, there is a substantial body of literature showing that dietary fibers, in particular soluble fibers, decrease blood cholesterol concentrations and may thereby modify the risk of coronary artery disease (7) and that dietary fiber may affect risk of large bowel cancers through mechanisms such as altering bile acid metabolism, increasing fecal bulk, or decreasing gut transit time (8).

Recently, attention has also focused on the possible roles of factors other than fiber that are contained in cereals and legumes and that may alter the risk of chronic diseases. Examples include vitamin E; B vitamins such as folic acid and minerals such as selenium that have not been added to refined flour products; and compounds with estrogenic activity, such as isoflavones or lignans (9). Because many of these factors occur together in nature and are relatively concentrated in whole foods, there has been interest in the possible differences between whole and refined grains in relation to chronic disease risk. In addition, cereal grains and their products are among the most commonly consumed items and are a staple in most human diets. Given the importance of cereals as a food, and the potential mechanisms

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relating cereal intake to decreased risk of chronic diseases, a number of epidemiologic studies have examined the association of these factors with disease risk. This article reviews the recent evidence from epidemiologic studies relating dietary fiber, whole grains, or legumes to the risk of chronic diseases.

**DIETARY FIBER AND HEART DISEASE**

Although the major focus of most epidemiologic studies of diet and heart disease has been the role of dietary lipids, there is also a substantial epidemiologic history of investigations regarding dietary fiber. After the initial observations of Trowell (4), several prospective cohort studies investigated the association of dietary fiber with heart disease (Table 1). The earliest of these, a 10- to 20-y follow-up of 337 British male bank and bus employees, reported a striking inverse association of total and cereal fiber intake with coronary artery disease incidence (10, 18). Other studies conducted in Netherlands (11); Framingham, MA (19); and Rancho Bernardo, CA (13) reported inverse associations between coronary artery disease and dietary fiber or carbohydrates from sources other than sugar or starch. However, in only one of these studies (13) was the association with dietary fiber controlled for energy intake.

In epidemiologic studies of diet, total energy intake is usually a confounder of diet-disease associations because intakes of almost all dietary factors are highly correlated with energy intake (20). This is simply because the more food one eats, the more of most dietary components one eats. It is also known that physical activity is inversely associated with heart disease risk and, in population studies, is a primary determinant of total energy intake (21). Thus, in studies in which dietary fiber intake is not controlled for energy intake, it is not clear whether observed inverse associations between fiber intake and heart disease risk are in part attributable to differences in energy expenditure. This is underscored by the observation that in most prospective epidemiologic studies of diet and heart disease, total energy intake is inversely associated with risk of heart disease (10–19).

One of the first prospective studies to examine the association of dietary fiber with coronary artery disease while controlling for energy intake was a study of brothers in Ireland and Boston (12). In this study, dietary fiber intake assessed in the late 1950s and early 1960s was inversely associated with risk of death from coronary artery disease after 20 y of follow-up, with men in the highest third of dietary fiber intake having a relative risk of coronary mortality of 0.57 compared with men in the lowest third. In 2 other prospective studies, one conducted in Caerphilly, Wales (15) and the other a follow-up of participants in the placebo arm of the Lipid Research Clinics Coronary Primary Prevention Trial (14), inverse associations between dietary fiber intake and coronary artery disease were observed. However, unlike the findings of the Ireland-Boston Diet-Heart Study (12) or the Rancho Bernardo study (13), these associations were attenuated and no longer significant after controlling for energy intake.

In the 1980s, several large prospective studies of diet and disease were established. Because enough time passed for these studies to have accrued reasonable numbers of events, several reports about the associations between dietary factors and heart disease risk in these studies have been published (16, 17, 22–24). In 1996, investigators from 2 of these studies reported associations between dietary fiber and heart disease risk. In one of these studies, a 6-y follow-up of 43757 male US health professionals, it was observed that men in the highest quintile of dietary fiber intake had a relative risk of myocardial infarction of 0.64 (95% CI: 0.47, 0.87) compared with men in the lowest quintile of intake (17). In further analyses, this association was found to hold true primarily for insoluble fibers and not soluble fibers, and for cereal fiber more strongly than for fiber from vegetables or fruit. The other study was a follow-up of participants in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (16). In this study, dietary fiber was inversely associated with coronary artery disease incidence; this association was strongest for soluble fiber and vegetable fiber sources, but was present for insoluble fiber and cereal and fruit fibers as well.

Preliminary analyses in a third, large, prospective epidemiologic study suggest that dietary fiber is inversely associated with risk of death from coronary artery disease (L. Kushi et al, unpublished observations, 1998). In this prospective study of 31284 postmenopausal women in Iowa, the relative risk of death from coronary artery disease was 0.76 (95% CI: 0.55, 1.05) among women in the highest quintile of dietary fiber intake compared with those in the lowest quintile. As in the study of male health professionals, this association was stronger with insoluble than soluble fiber and with fiber from cereals than fiber from vegetables, fruit, or legumes. In this study and 2 other prospective cohort studies (16, 17), these associations were apparent after controlling for total energy intake. Taken together, these prospective cohort studies provide remarkably consistent evidence that dietary fiber is likely to be inversely associated with risk of heart disease.

**DIETARY FIBER AND CANCER**

**Colorectal cancer**

As noted previously, the hypothesis that dietary fiber may decrease the risk of colorectal cancer was initially proposed by Burkitt (3). Since then, dietary fiber has been among the more frequently investigated dietary factors in studies of the etiology of colorectal cancer. Most of the analytic epidemiologic studies on this topic have been case-control studies, and these have been the subject of reviews (25, 26). In one such review, it was noted that 11 of 17 case-control studies of dietary fiber and colon cancer found an inverse association (25).

Howe et al (27) published one summary of these case-control studies, based on a combined analysis of original data from 13 such studies. This combined analysis included 5255 subjects with colorectal cancer and 10349 control subjects from studies conducted in Argentina, Australia, China, Singapore, Belgium, Greece, Spain, Canada, and the United States. Overall, there was a strong inverse association of dietary fiber intake with risk of colorectal cancer. The relative risks of colorectal cancer for subjects in the lowest quintile to subjects in the highest quintile of fiber intake were 1.0, 0.79, 0.69, 0.63, and 0.53 (P trend < 0.0001). This association remained after adjustment for other dietary factors that are correlated with fiber intake and may influence the risk of this cancer, such as vitamin C and β-carotene. This inverse association was highly consistent; it was observed in all but one (28) of the individual case-control studies included in this analysis and was found in case subsets, including subjects with cancers of the right-sided colon, left-sided colon, and rectum.

The combined analysis by Howe et al (27) was based on studies that had been completed before 1989. Since then, several
TABLE 1
Relative risk (RR) of coronary heart disease (CHD), comparing high and low dietary fiber intakes, in prospective epidemiologic studies.

<table>
<thead>
<tr>
<th>Study and location</th>
<th>Cohort</th>
<th>Age range at baseline</th>
<th>Study period</th>
<th>CHD events</th>
<th>Comparison</th>
<th>RR (95% CI)</th>
<th>P trend</th>
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<tr>
<td><strong>Total dietary fiber</strong></td>
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<tr>
<td>Morris et al (10), United Kingdom</td>
<td>337 M</td>
<td>30–67</td>
<td>1956–1976</td>
<td>45 events</td>
<td>Highest compared with lowest third</td>
<td>0.32&lt;sup&gt;4&lt;/sup&gt;</td>
<td>&lt;0.005&lt;sup&gt;5&lt;/sup&gt;</td>
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<tr>
<td>Kromhout et al (11), Zutphen, Netherlands</td>
<td>871 M</td>
<td>40–59</td>
<td>1960–1970</td>
<td>37 deaths</td>
<td>Highest compared with lowest fifth</td>
<td>~0.26&lt;sup&gt;6&lt;/sup&gt;</td>
<td>NS</td>
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<tr>
<td>Kushi et al (12), Boston and Ireland</td>
<td>1001 M of Irish descent</td>
<td>29–72</td>
<td>1959–1982</td>
<td>148 deaths</td>
<td>Highest compared with lowest third</td>
<td>0.57 (0.33, 0.97)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Khaw and Barrett-Connor (13), Bernardo, CA Men</td>
<td>356</td>
<td>50–79</td>
<td>1972–1985</td>
<td>42 deaths</td>
<td>Per 6-g increment</td>
<td>0.85 (0.64, 1.11)</td>
<td>0.15</td>
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<tr>
<td>Women</td>
<td>503</td>
<td>50–79</td>
<td>1972–1985</td>
<td>23 deaths</td>
<td>Per 6-g increment</td>
<td>0.67 (0.45, 1.00)</td>
<td>0.05</td>
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<tr>
<td>Combined</td>
<td>859</td>
<td>50–79</td>
<td>1972–1985</td>
<td>65 deaths</td>
<td>Per 6-g increment</td>
<td>0.79 (0.63, 0.98)</td>
<td>0.03</td>
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<tr>
<td>Humble et al (14), United States</td>
<td>1801 M</td>
<td>35–60</td>
<td>1973–1983</td>
<td>249 events</td>
<td>Highest compared with lowest fifth</td>
<td>~0.64 (0.43, 1.00)&lt;sup&gt;7&lt;/sup&gt;</td>
<td>0.003</td>
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<tr>
<td>Pietinen et al (16), Finland</td>
<td>21 930 M, smokers</td>
<td>50–69</td>
<td>1985–1993</td>
<td>1399 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.84 (0.71, 1.01)</td>
<td>0.03</td>
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<td>Rimm et al (17), United States</td>
<td>43 757 M, health professionals</td>
<td>40–75</td>
<td>1986–1992</td>
<td>734 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.68 (0.52, 0.88)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pietinen et al (16), Finland</td>
<td>31 284 F</td>
<td>55–69</td>
<td>1986–1995</td>
<td>375 deaths</td>
<td>Highest compared with lowest fifth</td>
<td>0.76 (0.55, 1.05)</td>
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<td>Rimm et al (17), United States</td>
<td>43 757 M, health professionals</td>
<td>40–75</td>
<td>1986–1992</td>
<td>734 events</td>
<td>Per 10-g increment</td>
<td>1.07 (0.57, 2.02)</td>
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<td>Kushi&lt;sup&gt;7&lt;/sup&gt;, Iowa</td>
<td>31 284 F</td>
<td>55–69</td>
<td>1986–1995</td>
<td>375 deaths</td>
<td>Highest compared with lowest fifth</td>
<td>0.79 (0.58, 1.08)</td>
<td>0.30</td>
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<td><strong>Soluble fiber</strong></td>
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<td>Highest compared with lowest fifth</td>
<td>0.79 (0.66, 0.94)</td>
<td>0.004</td>
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<td>40–75</td>
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<td><strong>Insoluble fiber</strong></td>
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<td>50–69</td>
<td>1985–1993</td>
<td>1399 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.86 (0.72, 1.02)</td>
<td>0.07</td>
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<tr>
<td>Rimm et al (17), United States</td>
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<td>40–75</td>
<td>1986–1992</td>
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<td>Highest compared with lowest fifth</td>
<td>0.70 (0.50, 0.96)</td>
<td>0.05</td>
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<td><strong>Cereal fiber</strong></td>
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<td>50–69</td>
<td>1985–1993</td>
<td>1399 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.94 (0.79, 1.12)</td>
<td>0.32</td>
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<td>43 757 M, health professionals</td>
<td>40–75</td>
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<td>0.007</td>
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other case-control studies have supported an inverse association between dietary fiber intake and risk of colorectal cancer. For example, in a study conducted in Washington State, Meyer and White (29) observed that in both men and women, those with colon cancer were likely to consume lower amounts of dietary fiber than were the population-based control subjects. The risk of colon cancer among subjects in the highest quartile of dietary fiber consumption was about one-half that of subjects in the lowest quartile, which was similar to the estimate made in the combined analysis. In a case-control study conducted in Russia, Zaridze et al (30) noted similar inverse associations of cellulose intake with risk of colorectal cancer. In a large multicenter case-control study, Slattery et al (31) also observed inverse associations of dietary fiber with colon cancer risk. Thus, although not all case-control studies support an inverse association of dietary fiber intake with risk of colon cancer (28, 32), overall such studies provide substantial support for this association.

There have been relatively fewer prospective cohort studies of dietary fiber and colon cancer and these studies are more equivocal with respect to this association. The prospective studies on this association include the Nurses’ Health Study (33) and the Iowa Women’s Health Study (34). In these studies there was some suggestion that high intakes of dietary fiber may be associated with lower colon cancer risk, but the relative risks for high compared with low intakes were modest at \(0.8–0.9\) and were not significant. In the Health Professionals Follow-up Study, a prospective study in men, a possible inverse association between dietary fiber and colon cancer was no longer observed after adjustment for potential confounding factors (35). Two other prospective studies, one in Japanese-American men in Hawaii (36) and the other in Dutch civil servants (37), also failed to observe an association of dietary fiber with colon cancer risk.

The discrepancy between case-control studies and cohort studies on this topic is somewhat perplexing. It may be a result of differential recall of dietary habits by case subjects compared with control subjects in the case-control studies. For example, case subjects may have modified their diet because of their disease, and their current dietary patterns could influence their recall of past dietary habits. Alternatively, case subjects may be more likely than control subjects to recall dietary factors that they think are associated with their condition. The discrepancy may also be attributable to other dietary factors that are associated with fiber intake, such as fruit and vegetables or red meat. Both vegetables and fruits (38) and red meat (25, 39) have been consistently associated with colon cancer risk in studies, including cohort studies. Overall, the studies about fiber and colon cancer provide modest support for an association between dietary patterns involving higher fiber intake and reduced risk of colon cancer.

### Other cancers

The potential association of dietary fiber with breast cancer has also been investigated in numerous epidemiologic studies. In 1990, Howe et al (40) reported the results of a combined analysis of data from 10 case-control studies of breast cancer; the authors found a modest decrease in breast cancer risk \(0.85\) with an increase of \(20\) g dietary fiber/d. Some of the more recent case-control studies of dietary fiber and breast cancer reported an inverse association (41) and others reported no association (42, 43). Prospective cohort studies have provided a similar view of

### Table 1 (Continued)

<table>
<thead>
<tr>
<th>Study and location</th>
<th>Cohort</th>
<th>Age range at baseline</th>
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<th>CHD events</th>
<th>Comparison</th>
<th>RR (95% CI) (^2)</th>
<th>P trend</th>
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<tr>
<td>Vegetable fiber</td>
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<td>0.05</td>
</tr>
<tr>
<td>Kushi(^2), Iowa</td>
<td>31 284 F</td>
<td>55–69</td>
<td>1986–1995</td>
<td>375 deaths</td>
<td>Highest compared with lowest fifth</td>
<td>0.96 (0.71, 1.31)</td>
<td>0.71</td>
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<tr>
<td>Fruit fiber</td>
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<tr>
<td>Pietinen et al (16), Finland</td>
<td>21 930 M, smokers</td>
<td>50–69</td>
<td>1985–1993</td>
<td>1399 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.90 (0.75, 1.07)</td>
<td>0.11</td>
</tr>
<tr>
<td>Rimm et al (17), United States</td>
<td>43 757 M, health professionals</td>
<td>40–75</td>
<td>1986–1992</td>
<td>734 events</td>
<td>Highest compared with lowest fifth</td>
<td>0.81 (0.62, 1.06)</td>
<td>0.10</td>
</tr>
<tr>
<td>Kushi(^2), Iowa</td>
<td>31 284 F</td>
<td>55–69</td>
<td>1986–1995</td>
<td>375 deaths</td>
<td>Highest compared with lowest fifth</td>
<td>1.06 (0.76, 1.47)</td>
<td>0.89</td>
</tr>
</tbody>
</table>

\(^{1}\) MI, myocardial infarction.
\(^{2}\) Adjusted for multiple CHD risk factors unless otherwise noted.
\(^{3}\) Estimated from information provided in the study publication.
\(^{4}\) Crude RR.
\(^{5}\) Men who developed CHD consumed significantly lower amounts of dietary fiber per 1000 kcal (4.184 MJ) than men who did not develop CHD \((P < 0.005)\).
the possible association between dietary fiber and breast cancer. In the Nurses’ Health Study, there was little suggestion that dietary fiber is associated with risk of breast cancer (44), a finding similar to that seen in the Iowa Women’s Health Study (45) and in a cohort of postmenopausal women in New York (46). Only one such study, a nested case-control study in a Canadian population, supported a decreased risk of breast cancer with increased intake of dietary fiber (47). Overall, these studies suggest that if there is an association of dietary fiber with risk of breast cancer, it is likely to be a modest one.

Regarding other cancer sites, relatively few studies have reported on dietary fiber intake. One review highlighted the consistent inverse associations between fiber intake and pancreatic cancer that were observed in 5 of 6 case-control studies (48). Five of these studies (49–53) were conducted under the auspices of the International Agency for Research on Cancer and used similar methods to allow pooling of data. In the combined analysis of these pooled data, the relative risks of pancreatic cancer from lowest to highest quintiles of fiber intake were 1.0, 0.66, 0.56, and 0.42 (P trend < 0.01) (54). For cancers of other sites, reviews indicate relatively little evidence of an association with fiber intake, either because few studies have been reported or the findings have been null or inconsistent (55, 56).

WHOLE GRAINS AND CHRONIC DISEASE

Although there has been substantial interest in the role that dietary fiber may play in chronic disease risk, there has been comparatively little focus on cereals and whole grains, which are major contributors to dietary fiber intake in most diets (57). This lack of focus is not simply a result of attention to nutrients or chemical compounds rather than foods or food groups; for example, there have been numerous studies of vegetables, fruit, and cancer risk, a topic of several reviews published in the past decade (38, 58, 59).

There are relatively few studies of whole grains and coronary artery disease (60, 61). In one of these, a prospective study of Seventh-day Adventists, consumption of whole-wheat bread was associated with significantly reduced risk of nonfatal coronary artery disease compared with consumption of white bread (relative risk: 0.45; 95% CI: 0.28, 0.71) (60). In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, consumption of rye products was associated with decreased risk of coronary artery disease, with relative risks from lowest to highest quintiles of rye intake of 1.0, 0.87, 0.86, 0.79, and 0.75 (P trend = 0.02) (24). Rye is not only an important source of fiber, but in Finland, the whole grain, rather than the refined grain, is usually consumed. Similarly, consumption of breakfast cereals was associated with a lower risk of coronary disease in the Health Professionals Follow-up Study (relative risk: 0.83; 95% CI: 0.69, 0.99), but information was not presented as to whether the cereals were made of whole or refined grains (62). Finally, in a cohort study of British vegetarians (63), daily consumption of whole-meal bread was associated with a nonsignificant reduction in risk of coronary mortality of 0.85 (95% CI: 0.68, 1.06); however, consumption of bran cereals was not associated with reduced mortality from coronary artery disease.

Recent analyses from the Iowa Women’s Health Study also suggest that whole-grain intake is inversely associated with coronary mortality (64). In this study, 387 of 34,492 women enrolled in the study in 1986 and eligible for follow-up had died of coronary artery disease after 9 y of follow-up. The relative risks of coronary artery disease death among quintiles of whole-grain intake from lowest to highest intake were 1.0, 0.92, 0.69, 0.61, and 0.70 (P trend = 0.02) after adjustment for multiple coronary disease risk factors. This inverse association was also seen for consumption of dark bread and whole-grain breakfast cereal. The inverse association with whole-grain intake could not be attributed solely to dietary fiber intake. Although adjustment for dietary fiber intake attenuated the relative risk estimates, the association was still apparent (relative risks from lowest to highest: 1.0, 0.96, 0.75, 0.68, and 0.77 (P trend = 0.12).

Interestingly, there was no association of refined-grain intake with risk of coronary artery disease death in the Iowa study (relative risk = 0.97 for highest compared with lowest quintile of intake) (64). In the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study, there was also no association between coronary death and cereal products other than rye products (16). These observations suggest that there may be differences in the health benefits of whole-grain compared with refined-grain intake, and that benefits seen with whole grains are not simply a result of substitution for higher meat or fat intakes. As described by Slavin et al (8), there are several potential compounds (in addition to dietary fiber) with associated mechanisms by which whole-grain intake may reduce the risk of chronic diseases such as cancer and heart disease.

Because there has been little focus on cereal or grain intake per se in epidemiologic studies, most studies have not collected dietary data in a manner that allows separation of cereal consumption into whole-grain and refined-grain intake. A review by Jacobs et al (65) identified 14 case-control studies of cancer that included information on dietary exposures associated with whole-grain intake. Examples of these exposures included whole-grain bread or pasta (66, 67), whole-meal bread (68), brown bread (69), or nonwhite bread (70). In this review, 4 of 5 case-control studies of colorectal cancer indicated inverse associations with whole-grain intake; odds ratios were generally ~0.75 when comparing high with low whole-grain intake. All 7 case-control studies of stomach cancer found inverse associations with whole-grain intake, with odds ratios ranging from 0.37 to 0.79 when comparing high with low intake. The other 2 case-control studies, on endometrial cancer, also suggested inverse associations with whole-grain intake.

In addition to the studies included in the review by Jacobs et al (65), there have been several other case-control studies of cancer that have published information on risk associated with whole-grain intake. For example, one of the case-control studies of pancreatic cancer that was mentioned previously with regard to fiber intake also included information on both whole- and refined-grain intakes (50). At least 4 other case-control studies of pancreatic cancer also included information on whole-grain intake (71–74). Two of these studies reported inverse associations of whole-grain intake with risk of pancreatic cancer (odds ratios of 0.44 and 0.70 for high and low intake, respectively; 71, 74), whereas 1 reported no association (72). An additional large case-control study of colon cancer reported an inverse association with whole-grain intake in men, but not women (31). At least 2 case-control studies of breast cancer with information on whole-grain intake have also been published; one of these reported an inverse association with whole-grain intake (75) whereas the other found essentially no association (76). Additional case-control studies of ovarian cancer (77), soft tissue sarcoma (78), and non-Hodgkin lymphoma (79) also reported inverse associations with whole-grain intake; in these studies, odds ratios comparing high with low intakes ranged from 0.40 to
Several of these and other case-control studies of cancer have also reported on risk associated with intake of refined grains. In contrast to the generally inverse associations seen with whole-grain intake, refined grains tend to be associated with increased risk of cancer across these studies. For example, among the case-control studies of colorectal cancer, refined-grain foods such as pasta (66, 81) or starchy foods and flour products (82) were associated with increased risk of colorectal cancer. In the large case-control study of colon cancer, refined-grain products were also associated with increased risk (31). Similarly, white bread intake was positively associated with pancreatic cancer risk in 3 studies (71–74). Six of the 7 case-control studies of stomach cancer that were included in the review by Jacobs et al (65) on whole grains also reported associations with refined-grain foods (69, 70, 83–86). In these studies, various refined-grain foods, including white bread (83, 85, 86), pasta (69, 84, 85), or rice (presumed to be white) (84, 85) were associated with increased risk of stomach cancer. Only in a study conducted in Sweden was a refined-grain food (white bread) not associated with stomach cancer risk (70).

There have been relatively few prospective studies of refined or whole-grain foods and cancer risk. In one prospective study conducted in Japan, intakes of rice and wheat, both of which are usually consumed as refined grains, were inversely associated with risk of colorectal cancer (87). In this same cohort, these foods were not associated with risk of stomach cancer.

Overall, these studies indicate that consumption of whole-grain foods is associated with reduced risk of a variety of cancers and coronary artery disease, whereas refined-grain foods may be associated with increased risk. Differences in disease risk associated with whole-grain compared with refined-grain foods suggest that these findings are not due simply to the substitution of high-carbohydrate foods for high-fat or animal foods and also suggest that people can reliably distinguish refined from whole-grain foods. The observations in the Iowa Women’s Health Study regarding the associations with coronary artery disease (64) also suggest that these findings cannot be attributed solely to dietary fiber intake. The findings do suggest that increased consumption of cereal products may reduce the risk of these diseases, but these cereal products should be consumed as whole grains rather than the more commonly available refined grains. Recent findings from the Nurses’ Health Study (88) and the Health Professionals Follow-up Study (89) that linked the glycemic index of foods with risk of type 2 diabetes underscore the possibility that there may be other beneficial health effects of whole-grain foods that are not yet widely recognized.

**LEGUMES AND CHRONIC DISEASE**

Along with whole grains, legumes constitute another food group that has been relatively understudied in an epidemiologic context. Whereas legumes are also a source of dietary fiber—the relatively high soluble-fiber content of peas and beans was shown to lower blood cholesterol concentrations in feeding studies (7)—their effects on coronary artery disease have been investigated in only a few studies. Similarly, although there has been substantial interest in the role that soyfoods may play in the prevention of cancer (90) or heart disease (7), there is relatively little support from epidemiologic studies for this association. Because other articles in this supplement focus on the possible role of soyfoods and phytoestrogens in chronic disease prevention, this article will not discuss the topic further.

The role of legumes in cancer prevention is unclear. Most reviews on this topic generally indicate that among epidemiologic studies, about as many studies suggest an inverse association as a positive association between intake of legumes and cancer risk (38). In a recent report concerning the association of legumes with cancer risk, it was noted that 58 epidemiologic studies have examined this association (91). Of these, 29 reported a decreased risk with higher intake whereas 22 reported an increased risk. Overall, no conclusions concerning the role of legumes in cancer risk could be reached based on this literature (91).

**SUMMARY AND CONCLUSIONS**

There is substantial evidence that increased consumption of dietary fiber is associated with reduced risk of coronary artery disease. This has been observed in the majority of prospective cohort studies that have published information on this association, although in some of these studies the association was weakened by adjustment for energy intake and cardiovascular risk factors. Whether dietary fiber intake is also inversely associated with risk of cancer, particularly large bowel cancer, is less clear. Although there have been relatively consistent findings of an inverse association between dietary fiber intake and risk of colorectal cancer in case-control studies, the several prospective cohort studies on this topic have not confirmed these findings.

There is some interest in the possible role that whole-grain foods may play in reducing the risk of chronic diseases. In comparison with the focus on dietary fiber, however, this topic has been relatively understudied. According to reviews, studies that have reported on the associations of whole grains with cancer risk appear to almost uniformly indicate reduced risk associated with increased intake of whole grains (65, 80). Whether this is attributable to dietary fiber, some other factor that is present in greater abundance in whole grains, or a combination of such factors is not clear. However, whole grains contain numerous compounds with biological activities that may lower the risk of chronic diseases, and the concentrations of many of these compounds are greatly diminished during the refining process.

There is considerable interest in the role that legumes may play in the prevention of chronic diseases. Much of this interest has focused recently on the role of soyfoods, which appear to have hypcholesterolemic properties and may influence estrogen metabolism and thereby decrease the risk of hormone-dependent cancers. However, there have been relatively few studies that have focused on elucidating the effects of legumes on disease risk, and the epidemiologic studies that have addressed this question have often focused on the roles of other foods or nutrients and therefore have collected limited information on legume intake. Many of these studies are reviewed elsewhere in this supplement. More work is needed in this area before the nature of associations with cancer, heart disease, or other chronic conditions can be more clearly understood.

Overall, the evidence regarding grains, dietary fiber, and legumes supports the broad dietary guidelines that have been promulgated by various agencies and committees. Indeed, research findings suggest that recommendations to consume whole grains deserve greater prominence than is currently provided in most dietary recommendations. This shift in emphasis toward whole grains and away from refined-grain breads, cereals, and pasta or
grain products that are otherwise undefined has been advocated by others (92). For example, the Dietary Guidelines for Americans (93) and the food guide pyramid (94) mention whole grains only in the text that accompanies the recommendations, and also only in the context of dietary fiber intake. Although dietary fiber appears to be one component of whole grains that is associated with reduced risk of coronary artery disease, other factors, such as vitamin E and phytoestrogenic lignans, may also play important roles in the consistently observed inverse associations of whole-grain intake with risk of chronic diseases.

REFERENCES