

## Review

# Intake of Refined Carbohydrates and Whole Grain Foods in Relation to Risk of Type 2 Diabetes Mellitus and Coronary Heart Disease

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Recent survey data indicate that more than 50% of all adult Americans are overweight or obese. In parallel with this epidemic of weight gain in the general population, the incidence rate of type 2 diabetes mellitus (DM) is rapidly rising. Although their precise contributions are unclear, dietary factors are thought to affect body weight and the development of insulin resistance. Recent epidemiological data indicate that diets rich in high-fiber whole grains are associated with lower risk of coronary heart disease (CHD) and type 2 DM. These data are consistent with results from recent metabolic experiments, suggesting favorable lipid profiles and glycemic control associated with higher intake of whole grains, but not with refined grains. It seems prudent, therefore, to distinguish whole-grain rather than refined-grain cereal products for the prevention of chronic diseases.

### Key teaching points:

- The prevalence of obesity and type 2 DM is rising to epidemic proportions in the United States, although consumption of fats has decreased.
- Different types and amount of grains consumed may have different impacts on the occurrence of type 2 DM and CHD.
- Dietary glycemic load and insulin demand are functional concepts that should be applied in assessing the relative importance of refined carbohydrates and whole grain products in relation to type 2 DM and CHD risk.
- Replacing refined grains and potatoes with whole-grain and minimally processed grain products, along with increasing intake of fruits and vegetables, offers a simple strategy to lower dietary glycemic load and insulin demand that can ultimately reduce the risk of both type 2 DM and CHD.

## Introduction

Despite advances in the prevention and treatments of diabetes mellitus (DM) and cardiovascular diseases (CVD) in the last half of the 20th century, two of every five deaths in the United States are attributed to CVD or diabetes [1]. Together, these two diseases accounted for more than \$220 billion in direct medical costs in 1997 [2,3], 20% of all health-care expenditures [4]. Type 2 DM is indeed an epidemic of our time, affecting approximately 15 million individuals in the US alone, almost 8% of the US population [5]. Approximately 800,000 new cases were diagnosed in

2000, with ethnic minorities bearing the largest burden [6]. Worldwide, the number of people with diabetes is expected to rise from 135 million in 1995 to 300 million in 2025 [7].

Insulin resistance and progressive pancreatic beta-cell dysfunction are well-established fundamental steps in the pathogenesis of type 2 DM [8–13]. Accumulating metabolic and epidemiologic data also indicate that impaired insulin action and compensatory hyperinsulinemia often result in abnormal blood lipid patterns (i.e., elevations of triglycerides [TG] and low levels of high-density lipoprotein cholesterol [HDL]), as well as hypertension and other hemodynamic changes, which in

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turn cause coronary heart disease (CHD). Further, insulin resistance, obesity and hyperglycemia are associated with elevated plasma levels of C-reactive protein (CRP), an important component of the ongoing acute-phase responses of the body to various stimuli. Taken together, both metabolic and epidemiologic data suggest that insulin resistance is a common antecedent for both type 2 DM and CHD and may reflect a chronic adaptation of the immune system [14]. Dietary factors are thought to be important in affecting these conditions albeit uncertainties abound regarding their precise contribution(s) [15,16]. Until recently, dietary research has focused primarily on the effects of fats, and a high-fat diet has been implicated as the real villain responsible for these chronic diseases. Since the 1950s, the American Diabetes Association, the American Heart Association and other national agencies have recommended that a large portion of energy be obtained from carbohydrates [17,18]. However, both the quality and composition of dietary carbohydrates in our food supply have changed significantly over this period [19]. Many people in the US and other industrialized nations are increasingly consuming readily digested refined carbohydrates such as sugar-sweetened beverages, corn syrup, potatoes and processed grain products, although the impact of these changes in the quality of carbohydrates in the diet on risk of chronic disease remains uncertain.

In this brief review, I summarize prospective epidemiologic data examining the relation of carbohydrate quality with risk of type 2 DM and CHD. Although I emphasize the benefits of whole grain foods, I present a brief discussion of the concepts of glycemic index (GI) and glycemic load (GL), as they may help to illustrate an important mechanism by which whole grains exert their beneficial effects on lowering risk of type 2 DM and CHD. Detailed reviews regarding GI and GL as important functional measures for the biological effects of carbohydrates have recently been published elsewhere [15,20].

### **Refined Carbohydrates and Risk of Type 2 DM**

As a continuous progressive metabolic disorder, type 2 DM often begins with years of asymptomatic insulin resistance/hyperglycemia/compensatory hyperinsulinemia before it results in the “exhaustion” of pancreatic beta-cells that ultimately leads to an irreversible state of diabetes. The mechanism of this phenomenon is not entirely clear, and whether it results primarily from excessive secretion of insulin (beta-cell exhaustion) or “toxicity” of glucose to beta-cells has not been fully resolved. In theory, however, either mechanism would predict that a long-term exposure to a diet resulting in higher blood glucose levels and a greater demand for insulin would increase disease risk. Therefore, classifying foods according to physiologic effects obtained directly from metabolic experiments is useful in understanding the health effects of diets. Two functional classification systems have been de-

vised to provide this kind of information. The GI measures and ranks the impact of carbohydrates on postprandial plasma glucose [21], and the insulinemic index does the same for postprandial plasma insulin [22]. At present, relatively little data on the insulin index are available, and future metabolic studies are warranted to quantify the relative insulin responses to different foods; however, the correlation between glycemic and insulinemic responses has been reported to be high ( $r$  0.74 [22] to 0.90 [23]).

The GI depends largely on the rate of digestion and the rapidity of absorption of carbohydrates [24–27]. Use of these indices has shown that many complex carbohydrates induce glycemic and insulinemic responses nearly as high as pure glucose, casting doubt on the usefulness of the traditional simple vs. complex classification system that is based on chemical composition alone. The GI, however, cannot capture the entire glucose-raising potential of dietary carbohydrates because the blood glucose response is influenced not only by the GI value of a food but also by the amount of carbohydrate in the food. The concept of GL, defined as the product of the GI value of a food and its carbohydrate content, incorporates both the quality and quantity of carbohydrate consumed [28–30]. With white bread used as the reference standard food, dietary GL is essentially a standardized way of quantifying the glucose-raising effect of an actual serving of food or an overall dietary pattern. The concept of dietary GL can be better appreciated by data presented in Table 1 which lists GI and GL values per serving for the major carbohydrate-contributing foods consumed by participants in the Nurses’ Health Study in 1984 and their percent contribution of these foods to overall GL and carbohydrate intake. Cooked potato (mashed or baked), cold breakfast cereals and some beverages (including orange juice, fruit punch, and cranberry juice) had a relatively high dietary GL per serving, whereas fruits and vegetables provided a very low dietary GL per serving.

Several prospective cohorts have incorporated the concept of GI in assessing the relations between dietary carbohydrate and risk of type 2 DM. In the Nurses’ Health Study, the multivariate-adjusted relative risk (RR) of type 2 DM during six years of follow-up was 1.37 (95% confidence interval [CI], 1.09–1.71) for an increase in GI of 15 units and 1.47 (95% CI, 1.16–1.86) for extreme quintiles of dietary GL. Women with the combination of high dietary GL and low cereal fiber intake were at an even higher risk of type 2 DM (RR, 2.43; 95% CI, 1.12–5.27) [30]. In the Health Professionals Follow-up Study, the multivariate-adjusted RR was 1.37 (95% CI, 1.02–1.83) in six years of follow-up for extreme quintiles of dietary GL and 2.17 (95% CI, 1.04–4.54) for the combination of high GL and low intake of cereal fiber. In the Iowa Women’s Health Study, however, neither GI nor GL was related to risk of type 2 DM in six years of follow-up, although dietary fructose and glucose were significantly associated with increased risk [31].

**Table 1.** Dietary Glycemic Index and Glycemic Load for the Top 20 Contributors to Carbohydrate Intake among 75,521 US Female Nurses 38 to 63 Years of Age in 1984\*

Foods	Percent contribution of glycemic load	Percent contribution of carbohydrate	Glycemic index* (%)	Serving size	Grams of Carbohydrate per serving	Glycemic load serving
1. Cooked potatoes (mashed or baked)	8.0%	5.9%	102	1	37	38
2. White Bread	5.0%	4.3%	100	1 slice	13	13
3. Cold breakfast cereal	4.8%	4.0%	See individual cereal	½ cup	—	—
4. Dark bread	4.8%	3.9%	102	1 slice	12	12
5. Orange juice	4.5%	3.8%	75	6 oz	20	15
6. Banana	3.6%	3.1%	88	1	27	24
7. White rice	3.3%	3.5%	102	1 cup	45	46
8. Pizza	3.0%	2.7%	86	1 slice	78	68
9. Pasta	2.7%	2.4%	71	1 cup	40	28
10. English muffins	2.6%	2.3%	84	1	26	22
11. Fruit punch	2.6%	2.2%	95	1 can	44	42
12. Cola	2.5%	2.1%	90	1 can	39	35
13. Apple	2.3%	3.2%	55	1	21	12
14. Skim milk	2.2%	3.8%	46	8 oz	11	5
15. Pancake	1.9%	2.1%	119	2-4	56	67
16. Table sugar	1.8%	1.5%	84	2 tbsp	4	3
17. Jam	1.7%	1.7%	91	1 tbsp	13	12
18. Cranberry juice	1.6%	1.5%	105	1 can	19	20
19. French fries	1.5%	1.6%	95	4 oz	35	33
20. Candy	1.5%	1.6%	99	1	28	28
<b>Cereals</b>						
	% Contribution to total cereal intake					
1. Shredded wheat	12.6%	—	95	½ cup	38	36
2. Raisin bran	11.7%	—	88	"	41	36
3. Corn flakes	7.9%	—	114	"	24	27
4. Grape nuts	6.3%	—	96	"	23	22
5. Cheerios	4.7%	—	106	"	16	17
6. All-bran	3.3%	—	72	"	16	12
7. Total	3.1%	—	109	"	23	25
8. Wheaties	2.9%	—	109	"	23	26
9. Bran flakes	2.4%	—	74	"	33	24
10. Special K	2.3%	—	74	"	20	15

\* Standard reference is white bread, which has a glycemic index of 100% (all other glycemic index values are relative to white bread). Standard serving sizes are from USDA food composition table.

### Refined Carbohydrates and CHD Risk

High intake of carbohydrates induces hypertriglyceridemia mainly by enhancing hepatic synthesis of very low-density lipoprotein [32,33] and possibly by reducing lipoprotein lipase activity [34]. Among healthy people, a high refined-carbohydrate diet also reduces levels of HDL, a lipoprotein that is protective for CHD [35]. Many metabolic studies have shown that high-carbohydrate diets increase levels of fasting triglycerides [36], as well as cause persistent increases in plasma remnant lipoprotein cholesterol and remnant lipoprotein triglycerides [37]. High-carbohydrate diets also appear to increase fat accretion by the conversion of excess carbohydrate to triacylglycerols and the reduction of fat oxidation [38,39]. Aside from lipid abnormalities, hyperglycemia and hyperinsulinemia associated with high carbohydrate diet may also lead to hypertension, impaired fibrinolysis, as well as endothelial and inflammatory responses that are predictive of increased CHD risk [32,40-42].

Few prospective studies have directly related carbohydrate intake and incidence of CHD. Two cohort studies of men completed almost 20 years ago suggested a weak inverse association between carbohydrate intake and CHD. In the Honolulu Heart Study, McGee and colleagues documented 456 cases of CHD among 8,000 men of Japanese ancestry who were followed for 10 years [43]. Measuring diets at baseline with a single 24-hour recall, the investigators reported that intake of calories and carbohydrates was lower among men who later developed CHD than was the rest of the cohort participants. No statistically significant associations were found in multivariate analysis when both total calories and carbohydrates were included in the same model. In the Puerto Rico Heart Health Program, Garcia-Palmieri and coworkers measured baseline diets among 8,218 men using a 24-hour recall and found a statistically significant inverse association between carbohydrate intake and CHD [44]. Because the results were not

adjusted for total energy intake, the observed benefit could have derived from increased physical activity, a known protective factor for CHD that largely determines between-person variation in total energy intake. Moreover, neither study measured the quality of carbohydrates, as determined by dietary GI or conducted stratified analyses to examine the associations between carbohydrate intake and CHD risk among subgroups of men defined by level of body weight.

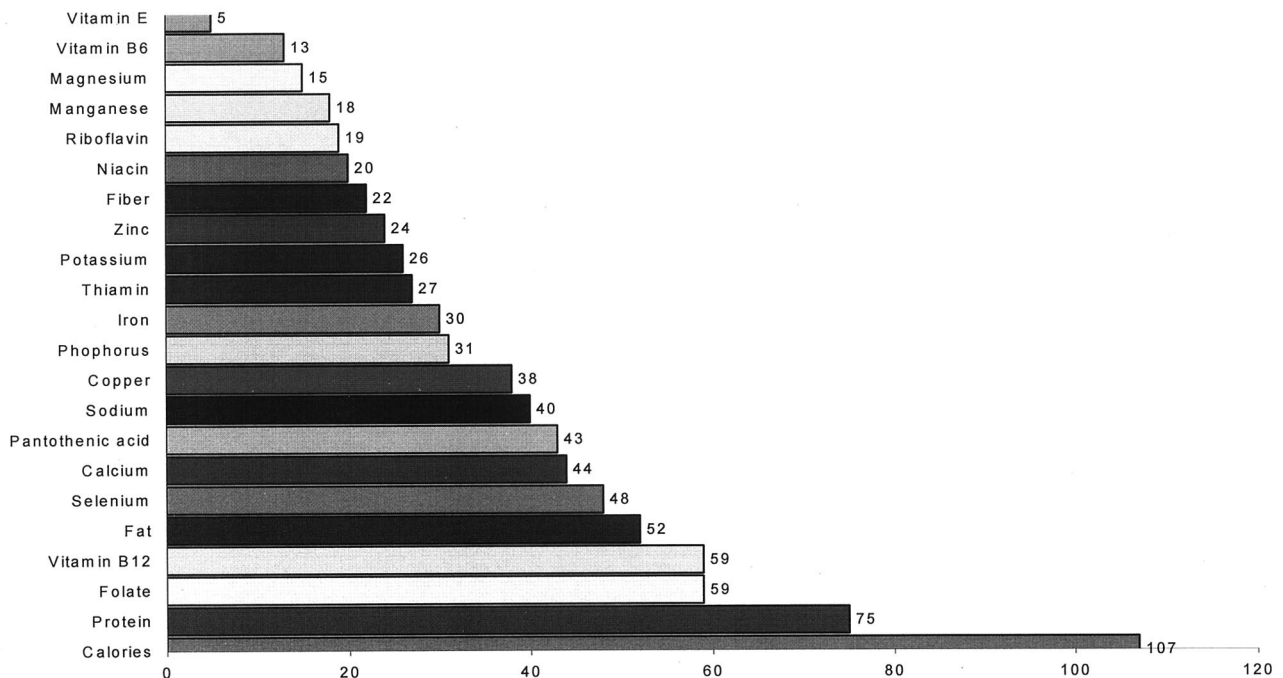
In a recent analysis of data from the NHS that assessed diets multiple times with a detailed semi-quantitative food frequency questionnaire, dietary GL was associated prospectively with risk of CHD after adjustment for age, smoking status, total energy intake and other dietary and non-dietary coronary risk factors. RRs from the lowest to highest quintiles of GL were 1.00, 0.98, 1.21, 1.49 and 1.98 (95% CI, 1.36–2.64 for the highest quintile; *p* for trend < 0.0001) over 10 years of follow-up [29]. In addition, classifying carbohydrates by GI, as opposed to the traditional classification of simple and complex, was a better predictor of CHD risk. A significant interaction between body mass index (BMI) and glycemic load was also observed. A high glycemic load diet did not appreciably increase the risk of CHD among lean women (BMI < 23), but was associated with a twofold increase in risk among women with an average or above-average BMI (BMI 23+), suggesting an important role of insulin resistance in modifying the effect of dietary GL on CHD risk. These findings are consistent with

results from recent metabolic studies showing that high-carbohydrate diets are associated with heightened degrees of dyslipidemia, especially among individuals prone to insulin resistance [36,45,46].

### Whole Grain Foods

Commonly consumed cereal grains include wheat, rice, corn, oats, barley and rye, with wheat and rice accounting for more than half of worldwide grain production [47]. In most developed countries, cereal grains are generally highly processed before use. In the US, for example, only 2% of the 150 pounds of wheat flour consumed per capita in 1997 was consumed as whole wheat flour [19], and the average American consumes fewer than one serving of whole grains a day.

Whole grains are generally low in saturated fat and high in dietary fiber, vitamins (especially the B vitamins), minerals and a wide range of phytochemicals that have been associated with improved long-term health. Milling removes most of the bran and much of the germ. The resulting refined grains have a higher starch content than the whole grains, but contain less dietary fiber and lower levels of vitamins, minerals, essential fatty acids and phytochemicals (Fig. 1). In addition, loss of the outer bran layer and pulverization of the endosperm allow for more rapid attack by digestive enzymes than is possible for whole grain products. Refined carbohydrates thus tend to cause



**Fig. 1.** Percentage of nutrients remaining after whole wheat flour is refined into white flour. Source: USDA food composition data, comparing values in whole grain wheat flour and white, unenriched wheat flour (<http://www.nal.usda/fnic>).

more rapid and larger increases in levels of blood glucose and insulin than do whole-grain products [48,49]. Because of their intact physical form, high content of viscous fiber and many enzymatic inhibitors, whole grains are digested and absorbed more slowly than refined grains and elicit relatively small postprandial glucose responses and thus relatively little insulin demand [50]. Whole grain products with intact bran and germ typically have lower GI values.

Many studies have examined the impact of specific components of whole grains, particularly dietary fiber, antioxidants such as vitamin E and minerals such as magnesium, on the development of chronic disease. This line of investigation has provided insight into the mechanisms because nutrients are most directly related to the physiology of human nutrition [51]. However, because of the chemical and physical complexity of whole grains, the potential benefits from consumption of whole grains may be derived from the balanced package of nutrients and antinutrients (such as phytic acid and tannins) they offer.

### **Whole Grains and Metabolic Markers**

A large body of evidence supporting the effects of whole grains on metabolic intermediates comes indirectly from studies of dietary fiber and other nutrients abundant in whole grains such as vitamins and magnesium. Dietary fiber, particularly soluble fiber, has been shown to decrease levels of postprandial glucose and concentrations of insulin and serum lipids [52–55]. In a recent randomized trial of 13 patients with type 2 DM [53], Chandalia and colleagues showed that changing from a low-fiber diet (8 g of soluble fiber and 16 g of insoluble fiber) to a high-fiber diet (25 g of soluble and 25 g of insoluble fiber) reduced 24-hour plasma glucose by 10% and insulin concentrations by 12%. The high-fiber diet also lowered concentrations of total cholesterol and fasting TG by 7% and 10%, respectively. In the Coronary Artery Risk Development in Young Adults (CARDIA) study, a low-fiber diet was associated with higher fasting insulin levels and greater weight gain in 10 years of follow-up [55]. Only recently have epidemiologic studies directly examined the effects of whole grains on plasma metabolic markers. In epidemiologic studies, foods classified as whole grain products include cold breakfast cereals containing at least 25% whole grain or bran by weight, dark bread, popcorn, cooked oatmeal, wheat germ and brown rice [56,57]. This definition is less stringent than the one used by the FDA which specifies 51% whole grain by weight [58]. Undoubtedly, some degrees of misclassification may exist in these data. Nonetheless, several epidemiologic studies have consistently linked whole grain intake to lower fasting insulin and glycemic response [59–63]. In the Framingham Offspring Study of 2,943 men and women, fasting insulin concentrations were lower in those with a higher intake of whole grain foods (207.2 – 198 pmol/L comparing the lowest to the highest quintile of intake,  $p = 0.002$ ), after controlling for BMI and other confounding factors. The inverse association between

whole grain intake and levels of fasting insulin was especially evident among overweight participants, a finding that has been observed consistently in several epidemiologic studies and is consistent with the well-observed association between overweight and insulin resistance in metabolic studies. A significant inverse relation between whole grain foods and fasting insulin levels has also been observed in the CARDIA study of more than 3,500 young adults [63]. In a subsample of 466 adult men participating in the Health Professional Follow-up Study, a dietary pattern that included high intake of whole grains was inversely associated with plasma insulin concentrations [59]. In the Dietary Approach to Stop Hypertension (DASH) trial, a diet high in fruits, vegetables and whole grains significantly lowered blood pressure compared to a typical western diet [64]. In a randomized trial of six adults with diabetes, Jenkins and colleagues examined the metabolic effect of breads with different whole grain content and reported a significant trend to lower glycemic response with an increase in the proportion of whole cereal grains in the test breads. Lower *in vitro* digestibility of test breads associated with high whole grain content also was observed [50]. A recent cross-over study involving eleven overweight subjects found that their insulin sensitivity, as measured by the euglycemic hyperinsulinemic clamp, improved after six weeks on a whole grain diet compared with a refined grain diet, independent of body weight [62].

### **Whole Grain Foods and Obesity**

Obesity, particularly abdominal or visceral adiposity, has consistently been demonstrated as a fundamental cause of type 2 DM [65,66]. As discussed above, many of the potential beneficial compounds of whole grains are lost in the refining process (Fig. 1). Although many short-term metabolic trials relating high-fat diet to weight gain are available, few trials have examined directly the effects of whole grains, as opposed to refined grains, on body weight and weight changes. Also, no long-term clinical trial has ever been conducted to provide conclusive evidence of a direct effect of whole grains on body weight. Nor is there any prospective epidemiologic study directly linking intake of whole grains to body weight or weight changes. However, indirect evidence from both epidemiologic and short-term experimental studies suggests a potential role of a high-GI diet containing refined grains in the development of obesity [67,68]. In a recent review of feeding trials in humans, Roberts and Heyman [68] concluded that the consumption of low GI foods was directly associated with reduction in subsequent hunger and/or increased satiety which leads to lower voluntary energy intake. Although most of these trials lasted for only a single meal or a single day, they together suggest that long-term consumption of whole grain products that are low in GI may increase satiety and reduce energy consumption and, thus, contribute to weight loss, especially among susceptible individuals (e.g., sedentary or overweight subjects). Several epidemiologic studies of dietary fiber also suggested that intake

of whole grains, but not of refined grains, was inversely associated with body weight and fat distribution [55,69]. The inherent high fiber content of most whole grain foods may help prevent weight gain by increasing appetite control through delaying carbohydrate absorption [70]. Alternatively, the lower postprandial glucose and insulin levels associated with higher whole grain intake may lead to weight loss, especially among overweight or obese individuals [61]. In this respect, components in whole grains such as fiber, magnesium and vitamin E have been associated with improved insulin sensitivity in metabolic studies [71–76]. Nevertheless, the correlation between dietary fiber and GI is modest ( $r = -0.23$ ) [77], and only approximately 21% of the GI variation can be explained by dietary fiber, suggesting other important factors in determining the glycemic effects of foods [78]. Two lines of evidence need to be pursued further in future studies, however. First, the inverse association between intake of whole grains and weight changes needs to be demonstrated prospectively in epidemiologic studies of large populations. Second, large and long-term intervention trials are necessary to assess the effects of whole grains versus refined grains on weight loss or weight maintenance in both overweight and normal-weight individuals.

### Whole Grain Foods and Risk of Type 2 DM

To date, only three prospective cohort studies using food frequency questionnaires for dietary assessment have examined the association between diets rich in whole grain foods and the development of type 2 DM.

In the Iowa Women's Health Study, 1141 incident cases of diabetes were self-reported over a six-year follow-up period in a prospective cohort of 35,988 healthy postmenopausal women. After adjustment for age, total energy intake, BMI, waist-to-hip ratio, education, cigarette smoking, alcohol intake and physical activity, intakes of total carbohydrates and starch were not associated with risk of type 2 DM [31]. In contrast, intake of total grains, whole grains, dietary fiber, cereal fiber and magnesium showed significant inverse associations with incidence of type 2 DM. For example, women in the highest quintile of whole grain consumption (more than 33 servings per week) were 21% less likely to develop type 2 DM than were those in the lowest quintile (less than 13 servings per week). In a prospective cohort of 75,521 healthy female nurses aged 38 to 63 years in 1984, we confirmed 1,879 incident cases of type 2 DM over a ten-year follow-up period. After adjustment for age and total energy intake, no association was observed between total grain intake and risk of type 2 DM [79]. There was, however, a statistically significant inverse association between whole grain intake and risk of type 2 DM and a statistically significant positive association between refined grain intake and risk of type 2 DM. In a comparison of the highest and lowest quintiles of intake, the age- and energy-adjusted RRs were 0.62 for whole grain (95% CI, 0.53–0.71;  $p < 0.0001$  for trend) and 1.31 for refined grain (95% CI, 1.12–1.53;  $p =$

0.0003), respectively. Although additional adjustment for BMI, cigarette smoking, alcohol intake, family history of diabetes, use of multiple vitamins, use of vitamin E supplements and physical activity slightly attenuated these associations, they remained statistically significant. To examine the net effect of refined versus whole grain intake, we created a ratio by dividing refined grain intake by whole grain intake. After adjustment for age and total energy intake, risk of type 2 DM increased across ascending quintiles of this ratio. Women in the highest quintile (those who consumed relatively large amounts of refined grain and relatively small amounts of whole grain) had a 57% higher risk of type 2 DM than did those in the lowest quintile. The exclusion of type 2 DM cases that were reported during the first four years of follow-up had a negligible effect on the multivariate-adjusted risks, suggesting that the presence of subclinical disease at baseline did not bias the results. Because almost 80% of the cases of type 2 DM were in women with BMIs greater than 25 and because BMI was the major confounder, the authors further analyzed the association between the refined grain/whole grain ratio and risk of type 2 DM among women with BMIs above 25 and reported similar findings for this subgroup, with risk of type 2 DM increasing across ascending quintiles. In the Health Professional Follow-up Study of 42,898 men aged 40 to 75 years followed for 12 years, Fung *et al.* recently reported a RR of 0.63 (95% CI 0.51–0.76) associated with about three servings/day of whole grain intake, providing further evidence that a diet high in whole grains is associated with reduced risk of type 2 DM in men [80].

### Whole Grain Foods and CHD Risk

In the Iowa study, Jacobs *et al.* demonstrated a significant inverse relationship between whole grain intake and death due to ischemic heart disease. The age- and energy-adjusted relative risk of mortality from ischemic heart disease was 0.60 (95% CI, 0.45–0.81) for women in the highest quintile of whole grain intake (median 22.5 servings per week) compared with those in the lowest quintile (median 1.5 servings per week) [81]. Similar inverse age- and energy-adjusted associations were observed for dark bread and whole-grain breakfast cereals. In contrast, intake of refined grain was not associated with mortality due to ischemic heart disease.

Two complementary reports from the Nurses' Health Study lend further support to the hypothesis that a diet rich in whole grains offers protection against CHD. Wolk *et al.* demonstrated that women in the highest quintile of dietary fiber intake had half the age-adjusted risk for major CHD events (nonfatal MI or CHD death) of women in the lowest quintile [82]. After further controlling for other coronary risk factors, dietary factors and multivitamin use, the authors demonstrated that an increase in total dietary fiber intake of 10 g per day (the difference between the highest and lowest quintiles) was associated with a 20% decrease in CHD risk. This reduction was

attributed to cereal fiber; other sources of fiber were not associated with lower risk of CHD events. In a separate analysis of the same cohort after adjusting for age, cigarette smoking, BMI, use of postmenopausal hormones, alcohol intake, use of multivitamin and vitamin E supplements, physical activity and types of dietary fat, a 25% lower risk of CHD (nonfatal MI and CHD death) was observed among women who ate nearly three servings of whole grains a day compared with those who ate less than a serving per week [57]. This association was even stronger among women who had never smoked. The risk reduction associated with increased intake of whole grain products was independent of components of whole grain foods currently believed to be beneficial, including dietary fiber, folate, vitamin B<sub>6</sub> and vitamin E. A similar inverse relation between intake of whole grains and risk of ischemic stroke has also reported in this population [83].

### **Implications and Future Directions**

The hypotheses regarding the relationships between whole grains, refined carbohydrates and risk of type 2 DM and CHD are based on the current understanding of the roles played by insulin resistance in the pathogenesis of these diseases. As the emphasis on reducing fat intake has become more prevalent in the population, consumption of carbohydrate-dense foods has increased. As with fats, dietary carbohydrates are highly heterogeneous in chemical structure and biological functions. Yet, the increasingly prevalence of high glycemic foods, including potatoes and refined grains, has been associated with obesity, diabetes and CHD. The individual response to a given GL may also be influenced by the degree of underlying insulin resistance, which is in turn determined primarily by degree of adiposity, physical activity, genetics and other aspects of diet. Future studies should further examine whether those people who are sedentary, obese and insulin resistant are prone to the adverse effects of these high GL foods. Future studies should also examine the relations between dietary carbohydrates and biomarkers of insulin resistance such as levels of triglycerides, fasting insulin and various cytokines. A demonstrated direct association between these biomarkers and reported carbohydrate intake can provide insights into potential mechanisms as well as validation for self-reported intake disclosed on food frequency questionnaires.

In conclusion, the physiologic impact of different foods on serum glucose and insulin is of critical importance and must be carefully determined and quantified. Such information should be routinely incorporated in future epidemiological studies of diet and chronic diseases. Available data indicate that replacing refined grains and potatoes with whole-grain and minimally processed grain products, as well as increasing the intake of fruits and vegetables, is a simple strategy for lowering dietary glycemic load and insulin demand that may ultimately reduce the risk of type 2 DM and CHD.

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