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## Whole-grain foods, dietary fiber, and type 2 diabetes: searching for a kernel of truth<sup>1,2</sup>

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Tracing the historical development of a scientific concept is a difficult and often subjective exercise. In the field of dietary research, however, the possibility that something of physiologic importance is lost in the refining process was perhaps first addressed comprehensively in the book Refined Carbohydrate Foods and Disease—Some Implications of Dietary Fibre (1). In that classic text, Burkitt and Trowell attributed the drastic differences between disease patterns in Africa, England, and North America to the refining of plant foods. The term dietary fiber was coined to describe the plant cell walls removed during the refining process. The ecologic argument of Burkitt and Trowell rested primarily on their observation that African natives who ate a plantbased diet and had large stools containing undigested plant materials had a lower prevalence of coronary heart disease, diabetes, and cancer than did Westerners. This so-called fiber hypothesis as it relates to health and disease has since been examined in numerous basic, clinical, and population studies. Results from these studies collectively form the modern science of dietary fiber that serves as the basis on which many national authorities recommend a diet high in naturally occurring fiber (2, 3).

In this issue of the Journal, Montonen et al (4) add data to that body of evidence linking a greater intake of high-fiber, wholegrain foods to a lower risk of type 2 diabetes. In a prospective cohort of 4316 Finnish men and women aged 40-69 y who were followed for 10 y, an inverse association between the intake of whole-grain foods and the risk of type 2 diabetes was reported. A similar relation was also found for the intake of cereal fiber, but not for the intake of fiber from vegetables and fruit. The risk reduction observed by Montonen et al was  $\approx 35\%$  from the highest to the lowest category of intake. These results are in general accordance with findings obtained from several prospective cohort studies of men or women in the United States (5-10). When the data from these prospective cohorts are pooled (Figure 1), the summary estimate of relative risk is 0.70 (95% CI: 0.64, 0.76; P = 0.63 for heterogeneity). In theory, these observational data, despite quality and precision, cannot provide direct causal proof of the effects of whole grains in lowering the risk of type 2 diabetes, because confounding remains an alternative explanation in nonrandomized settings. Several randomized feeding trials provide some causal explanations, however, by linking the intake of whole-grain foods to favorable metabolic intermediates, including smaller postprandial responses of glucose and insulin, improved serum lipid profiles, and lower oxidative stress (11-15). Together, the consistent findings from the prospective studies of diverse populations and supporting data from metabolic trials strongly support the premise that an increased intake of wholegrain foods can lower the risk of type 2 diabetes (14).

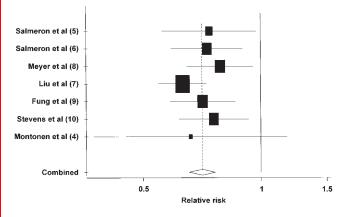
Despite much advancement in the field, confusion still abounds in defining dietary fiber and whole grains. In its original conceptualization, dietary fiber was viewed as a nutritional concept rather than as an exact description of a chemical component of food (16). However, in the process of deconstructing whole foods to understand their functions, and with the development of sophisticated chemical assays to quantify and isolate specific nondigestible carbohydrates, dietary fiber came to be considered as a group of chemicals rather than as an indicator for fiber-rich whole foods. Yet, because some experiments with the use of isolated chemical components of dietary fiber or "added fiber" have failed to produce desirable physiologic effects, interest has been rekindled in whole-grain foods as an important dietary intervention for health maintenance. Much research is summarized in a recent book devoted entirely to the subject (2).

Whole-grain foods are a unique source of dietary fiber in that plant cell walls constitute the complex matrices within which thousands of bioactive compounds coexist (17). In addition to the nonstarch polysaccharides of plant cell walls, whole-grain foods are rich in myriad vitamins, minerals, and other compounds that alone or in combination are likely to have significant health benefits (2). As opposed to intact grains, most whole grains are either finely milled or reconstituted after milling from the 3 conveniently defined components: the endosperm (starchy middle layer), the wheat bran (coarse outer layer) milled to a specific particle size, and the wheat germ (inner embryo layer). To lower the fat content, wheat germs are often heat-treated or in some instances may not be added back in the production process, although the final whole-grain products remain generally high in dietary fiber. For this reason, several epidemiologic studies have consistently defined whole grains as those products that comprise  $\geq 25\%$ whole-grain content or bran by weight (7-9, 14). In the United States, however, the Food and Drug Administration specifies whole-grain products as those meeting the criterion of 51% wholegrain content by weight.

In the report by Montonen et al, the intake of refined-grain foods was also inversely related to the risk of type 2 diabetes. This is a somewhat intriguing finding, as a higher intake of whole-grain foods was clearly associated with a lower intake of refined-grain foods, and previous large prospective studies consistently showed

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**FIGURE 1.** Estimated relative risks of type 2 diabetes as determined by comparing the highest and lowest categories of intake of high-fiber and whole-grain foods in 7 prospective studies and calculating their weighted average with the use of a fixed-effect model. The length of the horizontal lines indicates the width of the 95% CIs, and the size of the squares represents the specific weight or effect of the study on the final summary relative risks.

no benefit or even showed harmful effects of refined-grain products when they are eaten in place of fats or whole-grain foods (7-9, 14). Certain levels of misclassification may have introduced biases to the study of Montonen et al, which had only a small number of cases, and those biases led to some limitations in the results and their interpretations. As shown in Tables 2 and 3 in the report of Montonen et al, a greater intake of refined-grain foods was associated with a greater intake of total dietary fiber. This leaves one to wonder whether a greater intake of refined-grain foods was associated with a greater intake of fruit and vegetables. From the data presented, it was also not clear whether and to what degree refinedgrain foods still contained cereal fiber. It would be of interest to examine these data in greater detail with regard to the associations of refined-grain intake and other aspects of diet. Moreover, greater intake of refined-grain foods may be associated with greater levels of physical activity, which suggests that the inverse relation between refined-grain foods and the risk of type 2 diabetes may also be due to residual confounding by physical activity. Unfortunately, Montonen et al did not assess important variables such as physical activity and family history of diabetes. Distinguishing the biological effects of whole-grain and refined-grain products should be a priority in future work because current dietary guidelines implicitly advocate the intake of a large amount of refined grains.

In the nutrition field, there has been much discussion about the importance of functional foods—foods that affect physiologic functions—for quite some time. Fiber-rich, whole-grain foods may indeed have many overlapping physiologic effects, including favorable gastrointestinal function, improved lipid and glycemic profiles, and reduced oxidative stress (2). The most direct effect of whole-grain foods may be in the homeostatic control of blood glucose, and many functional effects can be attributed to the neuro-hormonal responses associated with the regulation of glucose homeostasis (18–20). The physical form and high fiber content of whole-grain foods and the presence of organic acids and enzyme inhibitors appear to work synergistically to affect digestion and absorption of glycemic carbohydrates (12, 21–24). More recently, studies have shown that the degree of gelatinization introduced in food processing is also extremely important in affecting the

ultimate glucose and insulin responses in vivo. Further research in quantifying the metabolic effects of different foods is clearly warranted, and basic research that follows the epidemiologic lead may eventually be fruitful.

Although total grain intake in the United States has increased in the past few years, much of that increased intake has been refined-grain products. Survey data indicate that Americans understand that whole grains are healthier than refined grains, but the average person eats less than one serving of whole grains per day. The challenge for the food industry is to make whole-grain products more appealing than refined-grain products. The challenge for public health professionals is to communicate to physicians, patients, and the general population the message that increased consumption of naturally occurring highfiber or whole-grain foods may prevent type 2 diabetes, without seeming to encourage excess intake of refined-grain products. At the individual level, the challenge is to develop habits to increase wholegrain intake such as substituting whole-wheat bread for white bread when making a sandwich. Developing such a simple habit may have \$ long-term health benefits.

## REFERENCES

- 1. Burkitt D, Trowell H, eds. Refined carbohydrate foods and disease: some implications of dietary fibre. London: Academic Press, 1975.
- Marquart L, Slavin JL, Fulcher RG, eds. Whole-grain foods in health and disease. St Paul, MN: American Association of Cereal Chemists, Inc, 2002.
- 3. US Department of Agriculture. Nutrition and your health: dietary guidelines for Americans. Washington, DC: US Government Printing Office, 2000.
- Montonen J, Knekt P, Järvinen R, Aromaa A, Reunanen A. Wholegrain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr 2003;77:622–9.
- Salmeron J, Ascherio A, Rimm EB, et al. Dietary fiber, glycemic load, and risk of NIDDM in men. Diabetes Care 1997;20:545–50.
- Salmeron J, Manson JE, Stampfer MJ, Colditz GA, Wing AL, Willett WC. Dietary fiber, glycemic load, and risk of non-insulindependent diabetes mellitus in women. JAMA 1997;277:472–7.
- Liu S, Manson JE, Stampfer MJ, et al. A prospective study of wholegrain intake and risk of type 2 diabetes mellitus in US women. Am J Public Health 2000;90:1409–15.
- Meyer F, Bairati I, Dagenais GR. Lower ischemic heart disease incidence and mortality among vitamin supplement users. Can J Cardiol 1996;12:930–4.
- Fung TT, Hu FB, Pereira MA, et al. Whole-grain intake and the risk of type 2 diabetes: a prospective study in men. Am J Clin Nutr 2002; 75:535–40.
- Stevens J, Ahn K, Juhaeri, Houston D, Steffan L, Couper D. Dietary fiber intake and glycemic index and incidence of diabetes in African-American and white adults: the ARIC study. Diabetes Care 2002;25: 1715–21.
- 11. Jenkins DJ, Wolever TM, Jenkins AL, et al. Low glycemic response to traditionally processed wheat and rye products: bulgur and pumpernickel bread. Am J Clin Nutr 1986;43:516–20.
- Chandalia M, Garg A, Lutjohann D, von Bergmann K, Grundy SM, Brinkley LJ. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med 2000;342:1392–8.
- 13. Jang Y, Lee JH, Kim OY, Park HY, Lee SY. Consumption of whole grain and legume powder reduces insulin demand, lipid peroxidation, and plasma homocysteine concentrations in patients with coronary artery disease: randomized controlled clinical trial. Arterioscler Thromb Vasc Biol 2001;21:2065–71.
- Liu S. Intake of refined carbohydrates and whole grain foods in relation to risk of type 2 diabetes mellitus and coronary heart disease. J Am Coll Nutr 2002;21:298–306.

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- Pereira MA, Jacobs DR Jr, Pins JJ, et al. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. Am J Clin Nutr 2002;75:848–55.
- 16. Goodlad RA, Englyst HN. Redefining dietary fibre: potentially a recipe for disaster. Lancet 2001;358:1833–4.
- Englyst HN, Quigley ME, Hudson GJ. Definition and measurement of dietary fibre. Eur J Clin Nutr 1995;49(suppl):S48–62.
- Liu S, Manson J. Dietary carbohydrates, physical activity, obesity, and the 'metabolic syndrome' as predictors of coronary heart disease. Curr Opin Lipidol 2001;12:395–404.
- Willett W, Manson J, Liu S. Glycemic index, glycemic load, and risk of type 2 diabetes. Am J Clin Nutr 2002;76(suppl):274S–80S.
- 20. Ludwig DS. The glycemic index: physiological mechanisms relating

to obesity, diabetes, and cardiovascular disease. JAMA 2002;287: 2414–23.

- Jenkins DJ, Josse RG, Jenkins AL, Wolever TM, Vuksan V. Implications of altering the rate of carbohydrate absorption from the gastrointestinal tract. Clin Invest Med 1995;18:296–302.
- 22. Englyst KN, Englyst HN, Hudson GJ, Cole TJ, Cummings JH. Rapidly available glucose in foods: an in vitro measurement that reflects the glycemic response. Am J Clin Nutr 1999;69:448–54.
- Jenkins DJ, Wesson V, Wolever TM, et al. Wholemeal versus wholegrain breads: proportion of whole or cracked grain and the glycaemic response. BMJ 1988;297:958–60.
- Foster-Powell K, Holt SH, Brand-Miller JC. International table of glycemic index and glycemic load values: 2002. Am J Clin Nutr 2002;76:5–56.