Dietary fiber and mortality: convincing observations that call for mechanistic investigations\textsuperscript{1–3}

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Dietary fiber is important for human health, and its role in the prevention of chronic diseases has been a topic of intensive research for many years. In 2009, after years of discussion, the Codex Alimentarius Commission finally adopted a worldwide definition of dietary fiber, and a new method fitted to the extended definition has been accepted by the Association of Analytical Communities. (1).

Fruit, vegetables, legumes, and grains are the main sources of soluble and insoluble dietary fiber, with a great structural and functional diversity. Dietary fiber from different food sources has different properties, such as increasing viscosity, gel formation, fermentability, and bulking, and it is well recognized that these properties cause different physiologic effects (2). For example, high-molecular-weight β-glucans are required to increase the viscosity of intestinal contents needed to obtain cholesterol-lowering effects (3). Insoluble fiber such as cellulose in lignified cell walls, on the other hand, will mainly contribute to bulking, which decreases bowel transit time and reduces intestinal exposure to procarcinogens (2). Some dietary fibers can readily be fermented by intestinal bacteria to generate short-chain fatty acids, which have been shown to affect hepatic insulin sensitivity and lipid synthesis and to modulate intestinal environment and perhaps appetite signaling (2).

In epidemiologic studies, dietary fiber, particularly cereal fiber (or whole grain), has consistently been associated with lower incidence of type 2 diabetes, cardiovascular disease (CVD), and some cancers, and lower incidence and mortality of CVD (2, 4–6). However, little is known about the role of dietary fiber in cause-specific mortality other than that from CVD and cancers, although studies have suggested protective associations for mortality related to inflammatory and respiratory diseases (7, 8).

In this issue of the Journal, Chuang et al (9) examined the associations of dietary fiber with mortality in the European Prospective Investigation into Cancer and Nutrition (EPIC) study, a large, prospective cohort study that includes participants from 10 European countries. Their study included 452,717 men and women, 23,582 of whom died during the mean follow-up time of 12.7 y. The large sample size and the wide range of fiber intake allowed investigations of total fiber as well as separate analyses for fiber from cereals, fruit, and vegetables in relation to total and cause-specific mortality. Dietary fiber intake was inversely associated with total mortality; the associations were similar for both men and women and were evident in most countries after careful adjustment for potentially confounding lifestyle and dietary factors, and they confirmed previous findings suggesting that dietary fiber is important for longevity (6–8).

Chuang et al (9) observed inverse associations for total fiber and circulatory diseases (for both men and women), which appeared to be caused by dietary fibers from cereals and vegetables. These results are not surprising because years of research have indicated that dietary fiber from these food sources have beneficial effects on CVD and its risk factors. The mechanisms underlying the protection may in part be mediated through LDL-cholesterol effects attributed to viscous dietary fibers (2, 3). However, protective associations between whole grain (rich in cereal fiber) and circulatory diseases have generally been shown in US populations where the main food source is wheat, which does not have cholesterol-lowering properties attributed to viscous fiber. This suggests that mechanisms other than direct cholesterol lowering must contribute to the protective associations observed. Recent findings from a large randomized controlled trial, in line with results from cross-sectional studies, showed that whole-grain wheat may prevent hypertension (10) and that this could contribute to the observed findings, although the mechanisms are unclear.

Chuang et al (9) also found that total fiber intake was associated with smoking-related cancers in both men and women. Again, it appeared that this association was attributed to cereal and vegetable fiber. In a recent large meta-analysis by Aune et al (4), total fiber (mainly from cereals) and whole grain were inversely associated with the risk of developing colorectal cancer (included in smoking-related cancers). Furthermore, in 2011, the World Cancer Research Fund changed the grading of the protective effect of dietary fiber on bowel cancer from “probable” to “convincing” on the basis of studies that have emerged since the World Cancer Research Fund Amercan Institute for Cancer Research’s 2007 Expert Report was published (11). The lower incidence of colorectal cancer caused by high cereal fiber and

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\textsuperscript{2} Supported by Nordforsk (Nordic Centre of Excellence programme HELGA).
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First published online June 6, 2012; doi: 10.3945/ajcn.112.040808.
whole-grain intake may partly explain the observed reduction in mortality risk for the smoking-related cancer group in Chuang et al’s study.

Interestingly, the study by Chuang et al (9) confirmed the recent findings by Park et al (8) and Jacobs et al (7), which showed an inverse association between fiber intake and death from respiratory diseases as well as for non-CVD, noncancer inflammatory diseases. Inflammation is a predominant pathophysiologic response in many chronic conditions such as rheumatoid arthritis, respiratory diseases, ulcerative colitis, diabetes, and neurodegenerative diseases, and it is causally linked to the progression of these diseases (7). Cereal fiber and whole grain have been associated with lower concentrations of inflammatory biomarkers in cross-sectional studies as well as in small intervention studies. Chuang et al suggest that short-chain fatty acids formed as a result of fiber fermentation may underlie the associations. The suggested mechanisms are intriguing but remain to be confirmed in human studies. Moreover, it is important to remember that cereal fiber is an essential component of whole grain and as such it may reflect whole-grain intake. Whole grain also contains several other components, which may have beneficial effects beyond cereal fiber.

In conclusion, the study by Chuang et al (9) adds further support to the health benefits of dietary fiber, mainly from cereals and vegetables. It showed inverse associations with total and specific mortality from circulatory diseases, essentially in line with previous studies, and confirmed more recent findings on non-CVD, noncancer inflammatory and respiratory diseases. Because total dietary fiber in a diet represents the sum (and perhaps interactions) of fibers with different properties and physiologic effects, the protective associations observed are very difficult to dissect and to attribute to specific mechanisms, particularly because the sources varied between the included countries. To obtain a better understanding of what mechanisms and which components may underlie protective associations, future studies should investigate specific fibers or at least their main food sources (as was done in the present study), and a range of new systems biology tools should be used on biological samples from such studies to gain more detailed insight. Meanwhile, it seems appropriate to continue to advise the general population to adhere to present dietary guidelines regarding vegetable intake and to increase their whole-grain intake by substituting refined grains with whole grains.

The author had no actual or potential conflicts of interest to report.

REFERENCES