

# Whole Grains and Health: from Theory to Practice—Highlights of the Grains for Health Foundation’s Whole Grains Summit 2012<sup>1,2</sup>

Nicola M. McKeown,<sup>3</sup> Paul F. Jacques,<sup>3</sup> Chris J. Seal,<sup>4</sup> Jan de Vries,<sup>5</sup> Satya S. Jonnalagadda,<sup>6</sup> Roger Clemens,<sup>7,8</sup> Densie Webb,<sup>9</sup> Lee Anne Murphy,<sup>10</sup> Jan-Willem van Klinken,<sup>11</sup> David Topping,<sup>12</sup> Robyn Murray,<sup>13</sup> Dennis Degeneffe,<sup>14</sup> and Leonard F. Marquart<sup>15\*</sup>

<sup>3</sup>Nutritional Epidemiology Program, Jean Mayer USDA Human Nutrition Research Center on Aging, Tufts University, Boston, MA; <sup>4</sup>Human Nutrition Research Centre, School of Agriculture Food and Rural Development, Newcastle University, Newcastle upon Tyne, UK; <sup>5</sup>HEALTHGRAIN Forum, Nutrition Solutions, Gorsel, The Netherlands; <sup>6</sup>Bell Institute of Health and Nutrition, General Mills, Golden Valley, MN; <sup>7</sup>University of Southern California, Los Angeles, CA; <sup>8</sup>Institute of Food Technologists, Chicago, IL; <sup>9</sup>Nutrition and Health Communications, Austin, TX; <sup>10</sup>Manitoba Agri-Health Research Network, Winnipeg, Canada; <sup>11</sup>PepsiCo, Barrington, IL; <sup>12</sup>Commonwealth Scientific and Industrial Research Organization (CSIRO), CSIRO Animal, Food and Health Sciences, Adelaide, Australia; <sup>13</sup>Grains and Legumes Nutrition Council, North Ryde, NSW, Australia; <sup>14</sup>Consumer Centric Solutions LLC, St. Paul, MN; and <sup>15</sup>Department of Food Science and Nutrition, University of Minnesota, St. Paul, MN; Grains for Health Foundation, St. Louis Park, MN

## Abstract

The Grains for Health Foundation’s Whole Grains Summit, held May 19–22, 2012 in Minneapolis, was the first meeting of its kind to convene >300 scientists, educators, food technologists, grain breeders, food manufacturers, marketers, health professionals, and regulators from around the world. Its goals were to identify potential avenues for collaborative efforts and formulate new approaches to whole-grains research and health communications that support global public health and business. This paper summarizes some of the challenges and opportunities that researchers and nutrition educators face in expanding the knowledge base on whole grains and health and in translating and disseminating that knowledge to consumers. The consensus of the summit was that effective, long-term, public-private partnerships are needed to reach across the globe and galvanize the whole-grains community to collaborate effectively in translating whole-grains science into strategies that increase the availability and affordability of more healthful, grain-based food products. A prerequisite of that is the need to build trust among diverse multidisciplinary professionals involved in the growing, producing, marketing, and regulating of whole-grain products and between the grain and public health communities. *J. Nutr.* 143: 744S–758S, 2013.

## Introduction

The 2012 Whole Grains Summit, held May 19–22, 2012, was the first meeting of its kind to convene >300 scientists, educators, food technologists, grain breeders, food manufacturers, marketers, health professionals, and regulators from around the

world. The goals of this meeting were to: 1) identify potential avenues for collaborative efforts; 2) discuss new approaches to whole-grains research and health communications; 3) support global initiatives to improve public health; and 4) generate new opportunities for product innovation and add value to the food

<sup>1</sup> Published in a supplement to *The Journal of Nutrition*. Presented at the 2012 Whole Grain Summit, held in Minneapolis, MN, May 19–22, 2012. The Summit was organized by the Grains for Health Foundation. In partnership with Academy of Nutrition and Dietetics, American Society for Nutrition, American Association of Cereal Chemists International, CSIRO, Grains and Legumes Nutrition Council, IFIC, Minneapolis Heart Institute Foundation, Minnesota Dietetic Association, National Pasta Association, Newcastle University, Pulse Canada, Sorghum Checkoff, USDA-ARS, USA Rice Federation, University of Manitoba, UW Center for Obesity Research, Wheat Foods Council, Wheat Marketing Center and Whole Grains Council. Financial support provided by: American Bakers Association, ADM, Bimbo Bakeries, Bob’s Red Mill, Cereal Partners Worldwide, CHS, ConAgra Mills, Corn Products International, De Vries Nutrition Solutions, Dow Agro Sciences, General Mills Bell Institute of Health and Nutrition, Health Grain Forum, Horizon Milling, IFT, Kraft Foods, Manitoba Agri-Health Research Network, Mars, Minnesota Obesity Center, MOM Brands, National Starch, Nestle, PepsiCo, UMN Healthy Foods Healthy Lives Institute, and Certified Foods. The views expressed in these papers are not necessarily those of the Supplement Coordinator or Guest Editors. The Supplement Coordinator for this

supplement was Len Marquart, Grains for Health Foundation, University of Minnesota. Supplement Coordinator disclosures: Len Marquart had no conflicts to disclose. This supplement is the responsibility of the Guest Editor to whom the Editor of *The Journal of Nutrition* has delegated supervision of both technical conformity to the published regulations of *The Journal of Nutrition* and general oversight of the scientific merit of each article. The Guest Editor for this supplement was Kevin Schalinske. Guest Editor disclosure: Kevin Schalinske had no conflicts to disclose. Publication costs for this supplement were defrayed in part by the payment of page charges. This publication must therefore be hereby marked “advertisement” in accordance with 18 USC section 1734 solely to indicate this fact. The opinions expressed in this publication are those of the authors and are not attributable to the sponsors or the publisher, Editor, or Editorial Board of *The Journal of Nutrition*.

<sup>2</sup> Author disclosures: N. M. McKeown, P. F. Jacques, C. J. Seal, J. de Vries, S. S. Jonnalagadda, R. Clemens, D. Webb, L. A. Murphy, J.-W. van Klinken, D. Topping, R. Murray, D. Degeneffe, and L. Marquart, no conflicts of interest.

\* To whom correspondence should be addressed. E-mail: lmarquart@umn.edu.

industry. Although this was the fourth Whole Grains Summit, this meeting was unique in terms of its vision for the future and the multidisciplinary nature of the participants. The summit brought together the various sectors and disciplines to address issues on how best to enable healthful, grain-based foods to more readily flow into the supply chain and provide easier access to consumers.

The summit's main objectives were to identify, understand, and discuss:

- Challenges and opportunities for filling research gaps relative to dietary guidance worldwide.
- Ways to build effective professional communications across disciplines and continents through engaging dialogue.
- Goals for global dietary guidance and how to identify ways to fill knowledge gaps where the research is not conclusive on whole grains and health.
- Consumer demand and supply chain challenges for increasing consumption of whole grains.
- Opportunities for reformulation or development of new whole-grain products.
- Effective approaches to link whole-grains research to communication and action.

This paper summarizes the state of whole-grains research in relation to health and disease, including the challenges and opportunities that educators face in disseminating that knowledge to consumers, barriers to increasing consumption of whole grains, food technology, and agricultural issues to be considered when striving to increase the amount of whole grains in food products.

## Background

The concept that an association exists between whole-grain consumption and health dates back to Hippocrates, who spoke favorably about "coarse" bread. Sylvester Graham advocated whole grains as a health food in the early 1800s. Dietary teachings of the Seventh Day Adventists religion, dating from the mid-1800s, included eating whole grains. In the United Kingdom, a medical practitioner named Thomas Allison advocated the consumption of unrefined flour and developed a whole-grain loaf specifically for health improvement. John Harvey Kellogg and Will Keith Kellogg, founders of Kellogg Company, were part of the modern day whole-grains movement. The practice of stripping the bran and germ from grain, leaving the much less nutrient-dense endosperm, occurred only in the last several hundred years. Prior to that time, whole foods were the norm and only whole grains were available for consumption. Later, refined-grain products were rare and available only for the wealthy. With the advent of steel roller milling, refined-grain flours became the norm in westernized countries. Whole grains today may include barley, bulgur, corn (including popcorn), rice, rye, oats, millet, sorghum, teff, triticale, wheat, and wild rice as well as the so-called "pseudo grains" amaranth, buckwheat, and quinoa.

Despite recent efforts in the US by the USDA through the 2010 U.S. Dietary Guidelines for Americans (DGA)<sup>16</sup> (1) and MyPlate (1) to encourage Americans to consume one-half of the recommended 6 servings of grain-based foods per day as whole

grains (48 g/d), the median intake of U.S. adults is about one-half serving or 8 g/d (3). Less than 1% of the U.S. population consumes the recommended intake of 3 servings (48 g/d) and 20% of individuals report consuming no whole-grain products (4). Jensen et al. (5) reported the median whole-grain intake among the men and women in the Health Professionals Follow-Up Study and the Nurses' Health Study II to be 22.3 g/d. In men, whole-grain intake ranged from 0.4 to 124 g/d (median, 23.4 g/d) and in women it ranged from 3.1 to 77 g/d (median, 21.9 g/d). By comparison, Sweden's adult population consumes an average 42 g/d of whole grains, Denmark 36 g (6–8), Britain 14–16 g, and France 7.3 g (9). However, gaps exist between recommendations and intakes in several countries for both children and adults (Table 1).

Greater incorporation of whole-grain foods into the diet can improve overall diet quality (Figs. 1 and 2). Using data from the NHANES, it was found that for both children and adults, diet quality improved with increasing consumption of whole grains. Specifically, intakes of most nutrients, including thiamin, riboflavin, vitamin A, and vitamin E were higher and sugars, SFAs, and sodium were lower among those who consumed  $\geq 3$  servings of whole grains/d (4,10) (Figs. 1 and 2). A recent survey conducted by the U.S. Academy of Nutrition and Dietetics determined that in the last 5 y, the indicated consumption of whole grains remained constant for 45% of those Americans surveyed and had decreased for 7% of the U.S. sample. Whereas 71% of American consumers believe they consume enough whole grains, 9 of 10 do not meet the whole-grains recommendation (11).

The 2010 DGA recommendation to consume more whole grains is based on the 2010 U.S. Dietary Guidelines Advisory Committee Report (3), which concluded that intake of whole grains protects against several major chronic diseases (1). As such, recommendations to increase whole-grain consumption require the food industry supply chain to grow, manufacture, and sell more whole-grain foods that promote health and contribute to an appropriate energy balance.

There has been an increase in chronic diseases worldwide in recent years, including cardiovascular disease (CVD) and diabetes as well as a rise in obesity and metabolic syndrome. National, regional, and global trends in abnormal blood sugar, metabolic syndrome, obesity, and diabetes are rising sharply worldwide (12–14). Chronic diseases now constitute the leading causes of global mortality and have commanded the attention of the United Nations and world leaders (15,16). Simultaneously, there is a growing body of evidence that dietary intake of whole grains may play a role in weight management and reducing the risk of CVD, diabetes, and hypertension (17).

Several countries in addition to the US recommend consumption of whole grains, including Australia, Austria, Bulgaria, Canada, China, Denmark, Germany, Greece, Hungary, Iceland, India, Ireland, Latvia, Mexico, Namibia, Netherlands, Norway, Oman, Singapore, Sweden, Switzerland, and the UK. However, far fewer provide a regulatory definition for whole grains or for whole-grain foods. The US has established a definition for what constitutes a whole grain, first developed in 1999 by the American Association of Cereal Chemists International and adapted by the FDA: "intact, ground, cracked or flaked fruit of the grain whose principal components, the starchy endosperm, germ and bran, are present in the same relative proportions as they exist in the intact grain" (18,19). The European HEALTHGRAIN Forum defined whole grains as consisting of the intact, ground, cracked, or flaked kernel after the removal of inedible parts such as the hull and husk. The

<sup>16</sup> Abbreviations: AR, alkylresorcinol; CHD, coronary heart disease; CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; DGA, Dietary Guidelines for Americans; RACC, reference amounts customarily consumed; tTga, tissue transglutaminase antibodies.

**TABLE 1** Dietary intake assessment of whole-grain intakes of adults reveals a large gap between recommendations and intakes<sup>1</sup>

Country	Cohort	Whole-grain intake recommendations	Whole-grain intake <sup>2</sup>		
			All	Female	Male
		<i>g/d</i>		<i>g/d</i>	
Denmark	HELGA	63–75	n/a <sup>1</sup>	31	41
Netherlands	Netherlands cohort	115	n/a	6.0 – 9.1	4.4 – 11.8
Norway	HELGA	70–90	n/a	44	n/a
Sweden	HELGA	70 – 90	n/a	35	49
UK	National Diet and Nutrition Survey	n/a	14 <sup>1</sup>	n/a	n/a
US	NHANES 1999–2004	48	12	n/a	n/a
	Health Professionals Follow-Up Study; Nurses Health Study II	48	22.3	21.9	23.4

<sup>1</sup> Source: references 4, 5, 7, 9, 118. n/a, not available.

<sup>2</sup> Values are medians or the range of means.

principle anatomical components, the starchy endosperm, germ, and bran, are present in the same relative proportions as they exist in the intact kernel (20). Establishing a universally accepted definition is a priority, because it would provide clarity for food manufacturers, aid in health promotion efforts, and protect consumers from false and misleading claims.

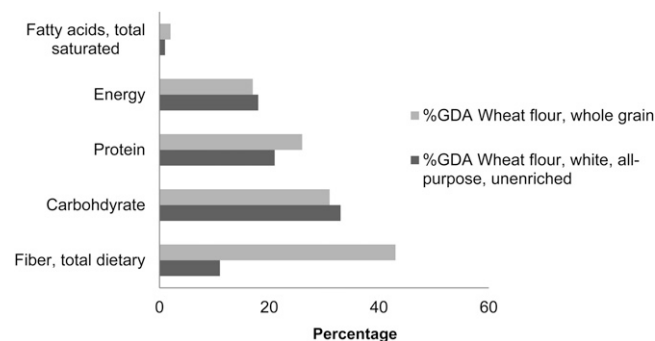
## Research on Whole Grains and Health

Findings from observational studies suggest that consumption of 2–3 servings of whole grains per day is sufficient to demonstrate beneficial health effects, such as reduced risk of CVD, type 2 diabetes, and overweight and obesity. The 2010 U.S. Dietary Guidelines Advisory Committee reviewed the available evidence and concluded that there was moderate evidence that whole-grain consumption is associated with a reduced risk of CVD and lower body weight and limited evidence that it is associated with a reduced risk of type 2 diabetes (21). The German Nutrition Society recently ranked the evidence on whole grains and health and determined that there is convincing evidence that whole-grain consumption reduces total and LDL cholesterol, probable evidence that it reduces the risk to type 2 diabetes, possible evidence that it reduces the risk of obesity in adults, but insufficient evidence that it reduces the risk of metabolic syndrome (22). However, more dietary intervention studies with appropriate end points and surrogate biomarkers are needed to define the scope and scale of the benefits. Observa-

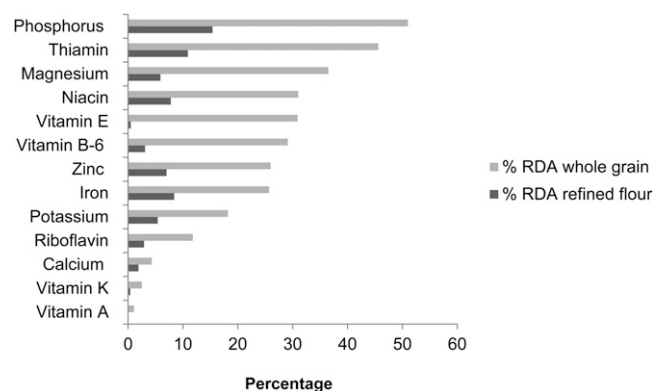
tional studies often are able to detect only small differences in health outcomes, because the highest whole grain intakes among most populations, especially U.S. populations, are relatively low. In addition, more studies are needed to better understand the mechanisms of action behind the association of health benefits with whole grains. There is also a pressing need to identify biomarkers for consumption of individual whole grains and whole grains collectively. Another major challenge to overcome for both epidemiological and dietary intervention studies is the lack of a comprehensive whole-grains database providing the whole-grains content of individual foods, which would allow a more accurate assessment of whole-grains intake.

**CVD.** Over the past several decades, CVD has risen to become the single largest cause of death worldwide, representing 30% of all deaths (17 million/y) (23). One of the earliest observational studies by Morris et al. (24) in 1977 found a strong inverse relationship between brown bread/fiber consumption and incident coronary heart disease (CHD). In 1992, Fraser et al. (25) studied a population of Seventh Day Adventists and found an inverse relationship between CHD and a preference for whole-wheat bread. A Finnish study of rye food intake by men and the large, prospective Iowa Women's Health Study found that whole-grain food intake was associated with a 25–30% reduced risk for CHD (26,27). Liu et al. (28) examined whole-grain intake and risk of CHD as part of the Nurses' Health Study and noted that whole-grain intake was associated with an almost 50% decreased risk of CHD. These early studies were among those that formed the basis for a whole-grain authoritative statement health claim initiated by General Mills, Inc. and approved by the FDA in July, 1999 (29), which says, "Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol, may help reduce the risk of heart disease and certain cancers." Whole-grain foods eligible for the claim have been defined by the FDA as foods that contain  $\geq 51\%$  whole-grain ingredients by weight per reference amounts customarily consumed (RACC) (29). Other than in the US, there are no approved whole-grain health claims. Since those early studies, interest in whole grains and health has increased and several epidemiological studies have demonstrated consistent inverse associations with disease, extending to diabetes (30) and inflammatory disease (31,32).

A meta-analysis of 7 prospective cohort studies with quantitative measures of whole-grains consumption and clinical cardiovascular outcomes indicated that consuming an average of 2.5 servings/d of whole grains was associated with a 21% lower



**FIGURE 1** Differences in the contribution of macronutrients from wheat flour (whole grain vs. white flour) to Guidelines Daily Amounts (GDA). The figure was prepared using data from U.S. National Nutrient Database for Standard Reference (119) and Healthgrain Forum (113).



**FIGURE 2** Differences in the contribution of micronutrients from wheat flour (whole grain vs. white flour) to RDA. The figure was prepared using data from U.S. National Nutrient Database for Standard Reference (119) and Healthgrain Forum (113).

risk of CVD events compared with an average low consumption of 0.2 servings/d (33). A systematic examination of 45 prospective cohort studies and 21 randomized controlled trials between 1966 and February 2012 found that compared with those who never or rarely consumed whole grains, those who consumed 48–80 g/d whole grains (3–5 servings/d) had a 21% lower risk of CVD (34). Among women diagnosed with type 2 diabetes, a protective association was observed between whole-grain consumption, particularly bran, and mortality from all causes and CVD-specific mortality (34). Published shortly after the summit, a systematic examination of longitudinal studies investigating whole-grains intake in relation to CVD suggested a 21% lower risk among those who consumed 48–80 g whole grains (3–5 servings) compared with never/rare consumers (35).

**CVD risk factors.** Hypertension is a major risk factor for CVD and several prospective studies have indicated a remarkably consistent association between whole-grain consumption and reduced blood pressure (36,37), even in young adults (38). Generally, as intake of whole grains increases, blood pressure decreases. When translated into whole-grain servings, consuming  $\geq 4$  servings/d of whole grains is associated with a 23% lower risk of incident hypertension (36).

Evidence from randomized, controlled trials has not been as consistent in supporting an association between higher whole-grain consumption and lower blood pressure. Two recent studies observed reductions in blood pressure in healthy, middle-aged participants consuming 48 g/d of whole grains for 3 or 12 wk (39,40). Tighe et al. (39) studied a group of middle-aged, healthy individuals in a randomized controlled trial, providing a 4-wk run-in period with a refined diet followed by a wheat or wheat + oats group for 12 wk. In this study, daily consumption of 3 portions of whole-grain foods significantly reduced systolic blood pressure. A smaller randomized, crossover pilot study of 14 healthy, normal-weight adults eating 48 g of whole-grain wheat for 3 wk found no change in other parameters reported. Importantly, this study observed that a lower systolic blood pressure observed after the whole grains intervention occurred in individuals who were normotensive on recruitment and therefore this was a clinically significant change (40). Consumption of breakfast cereals and incident hypertension was also assessed as part of the Physician's Health Study. Breakfast cereal consumption of  $\geq 7$  servings/wk, especially of whole-grains cereal, was associated with a significantly lower risk of hypertension in middle-aged adult males (41).

As part of the ongoing GrainMark dietary intervention study in the UK, blood pressure was found to be lower among participants when consuming 6 servings/d (96 g) of whole-grain wheat or rye than when consuming 3 servings/d (48 g), and both groups were lower than when no whole grains were consumed (42).

Not all studies have found a direct association between whole grains and blood pressure. The WHOLEheart study (43), a randomized, controlled dietary intervention of 316 overweight, healthy adults consuming  $<30$  g/d of whole grains for 16 wk, 60 g/d for 16 wk, or 60 g/d whole grain for 8 wk, followed by 120 g/d for 8 wk, found that whereas markers of cardiovascular risk (BMI, percentage body fat, waist circumference, fasting plasma lipid profiles, glucose and insulin, inflammatory markers and endothelial function) decreased at 8 and 16 wk with a greater consumption of whole grains, none changed significantly. However, participants appeared to include whole-grain foods as additions to, rather than substitutions for, refined grains in their regular diets. In addition, the participants reported increased energy intakes. It is possible that if isoenergetic diets had been maintained, a corresponding decrease in risk factors may have been observed consistent with other studies. Alternatively, the health effects of increasing whole-grain consumption might have been more pronounced if the participants were at an elevated risk for hypertension, type 2 diabetes, or metabolic syndrome. However, this study was conducted in healthy adults (44).

In a 12-wk trial of 79 overweight or obese postmenopausal women, participants consumed a diet in which whole grains replaced refined grains as part of an energy-restricted diet that was then compared with consumption of a diet consisting mainly of refined grains; serum total and LDL cholesterol increased with the refined-grains diet but not the whole-grains diet (45). In a study of 50 obese men and women with metabolic syndrome and following a hypocaloric diet with or without whole grains, only the group receiving whole grains experienced a significant reduction in C-reactive protein, a potentially important biomarker of transient inflammation and one of many factors that may indicate risk of CVD events (46). Whole-grains consumption may also lower serum concentrations of homocysteine, another predictor of CVD risk (47). In a small, clinical study of 11 overweight, hyperinsulinemic, nondiabetic men and women, Jacobs et al. (48) suggested that increased consumption of whole grains raised serum enterolactone concentrations. Enterolactone, the most abundant lignan in humans, may have the potential to reduce risk for chronic diseases, including CVD (49).

The summit concluded that the current evidence is strong and consistent to suggest that whole-grain consumption has a beneficial effect on decreased CVD risk and death from CVD, possibly via a reduction in total and LDL cholesterol and blood pressure. However, additional research is needed to identify other possible mechanisms of action, including improved glycemic control, insulin sensitivity, endothelial function, and reduced inflammation as well as elevated concentrations of enterolactone, which may have the potential to reduce the risk for several chronic diseases, including CVD (49).

**Weight management.** More than half a billion adults worldwide are overweight or obese and at least 2.8 million people die each year as a consequence (23). Sixty-five percent of the world's population lives in countries where overweight and obesity kill more people than underweight (50). Prospective epidemiological studies are quite consistent in showing a relationship between



whole-grain consumption and a lower BMI and improved weight regulation over time (51). However, whole-grain consumption often results in subtle differences in weight gain, rather than weight loss, and it is unclear whether whole-grains consumption is simply a marker of a healthier lifestyle or a unique factor favoring lower body weight.

It is possible that relatively small decreases in the digestible energy of whole-grain foods relative to refined grains account for the effect (52). This difference is largely due to the digestibility of starch, i.e., resistant starch, which accounts for a reduction of 2 kcal/g in the metabolizable energy. This could translate to significant differences in body weight, but long-term studies are required to evaluate the effect of whole grains on body weight regulation, weight gain, fat deposition, and appetite regulation.

As part of the Health Professionals Follow-up Study, researchers found that for every 40-g/d increment in whole-grain intake, weight gain was reduced by 0.49 kg over an 8-y period (53). The prospective Nurses' Health Study examined the intakes of dietary fiber and whole or refined grain products and weight gain over time and found weight gain to be inversely related to intake of high-fiber, whole-grain foods, but positively related to the intake of refined-grain foods (54). The systematic analysis by Ye et al. (35) revealed that whole-grain consumers experienced consistently less weight gain during the 8- to 12-y follow-up compared with never/rare consumers.

Weight-loss intervention trials have not been as encouraging, possibly because of the relatively small differential energy values of whole and refined grains. Several studies conducted in obese or overweight adults, lasting from 4 to 12 wk, reported no differences in weight loss in whole grain compared with control diets (46,55–57). Kristensen et al. (45) discovered no difference in body weight changes between overweight and obese postmenopausal women consuming either whole grains or refined grains, but the whole-grains group experienced a greater reduction in the percentage of fat mass. A study of obese men and women consuming hypocaloric diets found no difference in weight loss whether the participants consumed whole grains or refined grains (46). A small pilot study of 14 healthy, normal-weight adults consuming 48 g of whole grains daily for 3 wk revealed no changes in weight associated with whole-grains consumption (40). However, a randomized, controlled trial of 144 overweight and obese adults found that although weight loss did not differ between those consuming 2 portions/d of whole-grain ready-to-eat oat cereal or an energy-matched low-fiber food, those consuming the whole-grain cereal experienced a significant decrease in waist circumference (57). A cross-sectional examination of whole- and refined-grain intakes, waist circumference, and abdominal subcutaneous adipose tissue and visceral adipose tissue among Framingham Heart Study participants found that an increased intake of whole grains was associated with lower visceral adipose tissue in adults (58).

There is little research in children (59,60) to examine whole-grain intake and risk for chronic disease. However, a recently published study found that among children 2–7 y of age, those who consumed >1.5 servings/d of whole grains had a 40% lower risk of being obese compared with children who consumed <1 serving/d (61).

The evidence to date suggests that regular consumption of whole grains may aid weight regulation and lessen accumulation of abdominal adipose tissue. Several possible mechanisms have been suggested, including lower energy density of whole-grain-based foods, lower glycemic index, increased satiety signals via fermentation of nondigestible carbohydrates in the intestinal tract, modulation of intestinal microflora, and reducing insulin

secretion compared with refined grains (51,58). There is a need for long-term studies to evaluate the effect of whole grains on body weight regulation, weight gain, fat deposition, and appetite regulation.

**Diabetes.** The International Diabetes Foundation predicted that by 2030, almost 10% of the world's population will have diabetes (62). Consumption of whole grains has been associated with a reduced incidence of type 2 diabetes in several large prospective cohort studies (30).

A systematic review of the prospective Nurses' Health Studies I and II, which included almost 162,000 U.S. women enrolled without a history of diabetes, found a relative risk of 0.63 for developing type 2 diabetes over time when comparing the highest quintile of whole-grain intake with the lowest (30). When intake of bran and germ was delineated, associations for bran intake were similar to that for whole-grain intake, whereas no such association was observed for intake of germ. In the same paper, de Munter et al. (30) pooled data for 6 cohort studies that asserted a 2-serving/d increment in whole-grain consumption was associated with a 21% decrease in risk of type 2 diabetes after adjustment for potential confounders and BMI.

A recent systematic examination by Ye et al. (35) of 45 prospective cohort studies reported a 26% lower risk of type 2 diabetes among those consuming 48–80 g/d whole grains (3–5 servings) compared with never/rare consumers.

Higher whole-grain intake may improve intermediate markers of diabetes risk, such as fasting and postprandial measure of insulin and glucose. Several short-term intervention trials compared whole with refined grains on diabetes risk factors, but the results from these trials were inconsistent, perhaps due to variation in participant type (overweight, general population, diabetes, CHD, weight loss) or study duration. In one of the early intervention trials that compared whole grains with refined grains, Pereira et al. (63) found that overweight and obese adults consuming 6–10 servings/d of whole grains experienced 10% lower fasting insulin concentrations compared with those consuming the same number of daily servings of refined grains.

Jang et al. (47) randomly assigned 76 male patients with coronary artery disease to either a control diet or a diet containing 70 g of whole grains and legume powder each day for 16 wk. Men consuming the meal containing 70 g of whole grains and legume powder experienced reductions in serum glucose and insulin of 24 and 14%, respectively, based on fasting and 2-h postprandial glucose tolerance tests.

As part of the Sysdimet study in Finland, men and women with impaired glucose metabolism and at least 2 other features of metabolic syndrome participated in a 12-wk, parallel dietary intervention (64,65). Compared with those randomized to a control diet, those participants following a diet rich in whole grains (50% cereal grain products, whole grain snack bar) and low-insulin-response whole-grain products, bilberries, and fatty fish experienced improved glucose metabolism and improved markers of endothelial function and inflammation. The researchers concluded that the diet may contribute to a reduced risk of developing type 2 diabetes and possibly improve endothelial dysfunction and inflammation in high-risk persons.

Additional studies are needed to better understand the complex relationship that exists between whole grains and the risk of type 2 diabetes and identify potential mechanisms of action. Whole-grain consumption may reduce risk by lowering insulin and blood glucose concentrations and reducing inflammation.

**Colorectal cancer.** Colorectal cancer is the third most common cancer in men and the second most common cancer in women worldwide (66). The accumulated data suggest that diet is an important factor in determining risk. The U.S. FDA whole-grain authoritative statement health claim cited previously, which was allowed by the FDA in July, 1999 (19), includes cancer as well as heart disease. The evidence is less convincing for an association between consumption of whole grains and colorectal cancer than for whole grains and CVD. Among the >133,000 men and women who participated in the Cancer Prevention Study II Nutrition Cohort, no association was found between intake of whole grains and colon cancer risk. Quintiles of whole grain intake ranged from a low of 0.8 servings/wk to 14.5 servings/wk (67). Higher intakes of whole grains may be necessary to reduce the risk of developing colon cancer. A cohort study of 61,433 Swedish women found that those who consumed at least 4.5 servings/d (31.5 servings/wk) of whole grains compared with those who consumed <1.5 servings/d (10.5 servings/wk) had a 33% lower risk of colon cancer (68). Several studies have examined the association between whole-grain intake and a moderately reduced risk of colon cancer (69,70).

An earlier review and meta-analysis of case-control studies of whole-grain intake and cancer reported a significant inverse association between high intakes of whole grains and colon cancer and polyps (27). A systematic review of 6 prospective studies showed an increment of 3 servings/d of whole grains was associated with a 17% lower risk for colorectal cancer (71). It is possible that studying dietary patterns that include whole grains, such as the Dietary Approaches to Stop Hypertension (DASH), are relevant. Fung et al. (72) assessed the association between adherence to a DASH-style diet and risk of colorectal cancer among participants of the Health Professionals Follow-up Study and the Nurses' Health Study. Adherence to the DASH diet was associated with a lower risk of colorectal cancer.

Overall, there appears to be an inverse association between consuming whole grains and adhering to dietary patterns that include whole grains, and a reduced risk for colon cancer. Whole grains may reduce risk of colon cancer via synergistic effects of several antimutagenic and anticarcinogenic compounds they contain and by the action of SCFAs. This is supported by an animal study published after the summit that demonstrated opposition to genetic damage (a prerequisite for oncogenesis) by whole-grain, high-amylose wheat (73). This effect appeared to be through SCFAs produced by fiber fermentation, specifically butyrate. In addition, insoluble dietary fiber and lignans may adsorb or dilute potential carcinogens (74).

Most studies to date have relied on FFQs to assess dietary intake. However, measurement errors associated with the use of FFQs may obscure associations between dietary intake and risk of chronic disease, such as colon cancer. Based on memory, FFQs may either over- or underestimate actual consumption. Intervention studies to investigate the health-specific effects of whole grains on colon cancer may not be feasible given the long-term nature of cancer's development and progression. This explains in part the dependence on animal models to study the potential of dietary factors to modify colorectal cancer risk and suggests that findings to date may actually be conservative estimates of underlying risk reduction. Future studies should incorporate correction for measurement error in the analyses (71).

**Gastrointestinal health.** The intestinal tract is one of the more challenging organs of the body to maintain homeostasis because of its continuous exposure to pathogens and toxins. Several factors affect digestive health, including diet, environmental

factors, age, and genetics. Whole grains, principally nonstarch polysaccharides, oligosaccharides, and resistant starch, are the main dietary substrates for the bacterial species that ferment undigested dietary components in the intestinal tract (75). The principal products of this fermentation are SCFAs: acetate, propionate, and butyrate (75). The SCFAs appear to have specific roles in maintaining immune health, which, in turn, controls common pathogens and assists diarrhea management, colonic neuromuscular activity, and oncogenesis in the gut (75).

Fiber also plays a role in characterizing the microbiome in the gut and in modulating gastrointestinal motility. Among the other compounds in whole grains that can affect gastrointestinal health include phenolic acids, flavonoids, carotenoids, lignans, vitamin E, inulin, oligosaccharides, and  $\beta$ -glucan (74).

Several studies have found that daily consumption of whole-grain wheat (76), whole-grain maize (77), whole-grain oats (78), and soluble corn fiber (79) have a prebiotic effect on the human gut microbiota composition. It is likely the sum of the parts of whole grains contribute to gastrointestinal health (42). The large bowel microbiome of humans plays a prominent role in host health. Dietary strategies to manipulate that microbiome in a positive manner need to be identified (80).

**Epidemiological vs. intervention studies yield inconsistent findings.** Although there is a broad consensus on the population data, the results of intervention trials have not reproduced and supported the findings of epidemiological studies. Most interventions have been of short duration,  $\geq 4$  mo, and may not have been long enough to demonstrate long-term benefits. Short-term studies provide a glimpse of the relationship of whole grains to health but reveal little in terms of long-term risk reduction. Care must be taken in the interpretation of findings from small, short-term intervention studies, which often recruit only high-risk participants, including obese individuals and those with diabetes or metabolic syndrome, who may not be affected in the same manner by whole-grains consumption as lower risk individuals consuming whole grains over the long term.

Results from some studies also suggest that whole grains in isolation may not be as effective as when part of an overall healthful diet. Findings for healthful dietary patterns, of which whole grains are a part, are stronger than those for whole grains alone. In the Jang study (47), serum concentrations of homocysteine decreased by 32% in the dietary pattern group that included whole grains. Recent findings from the Coronary Artery Risk Development in Young Adults study found that during 20 y of follow-up, the correlation between a healthy dietary pattern, which included whole grains, and reduced clinical events was far stronger than that of whole grains alone (81).

Although there have been no long-term intervention trials with clinical outcomes for whole-grains intake and none are planned, the PREDIMED trial from Spain (82), a long-term, nutritional intervention study of almost 7000 individuals to assess the efficacy of the Mediterranean diet in the primary prevention of CVD, may provide some relevant findings regarding whole grains as part of a dietary pattern and health. The study, which was recently completed could serve as a template for future studies on the health benefits of whole grains. Although not all intervention studies have shown a positive association between whole-grain consumption and health parameters, no epidemiological or dietary intervention studies have demonstrated a negative or adverse effect of whole-grain intake. Even fewer studies have been carried out on the effects of whole-grain consumption on children's health and there are no

intervention studies on the primary risk reduction of obesity in children and adolescents through whole-grain food products (22).

There are inherent challenges in planning and conducting dietary intervention trials that make it difficult to study the long-term impact of whole grain consumption on health. Recruiting and screening participants is always challenging, but when studying whole grains, the research question should drive the selection of study participants, i.e., should they be healthy or metabolically unhealthy? Is the goal to study potential beneficial effects of whole grains (weight loss, lowering CVD risk, lowering blood pressure) or is it to study public health effects (reducing weight gain, lowering cholesterol concentrations and high blood pressure)? Should participants be normal weight, overweight, or obese? Should they be whole-grain “naïve,” i.e., they do not currently consume whole grains? Should they be free-living or should it be in a controlled setting? Another consideration is that blinding may not be possible for whole-grain foods because of texture and taste differences, and control groups may be exposed to whole-grain foods outside the parameters of the study.

A major challenge for both epidemiological and intervention trials is the lack of a valid whole-grain database that can be consistently applied to assess whole-grain intakes and allow for the comparison of study findings. The Harvard School of Public Health developed and continues to expand a database of whole-grain foods with the objectives of quantifying the whole-grain, bran, and germ components of foods; estimating the whole-grain composition of foods with and without bran and germ; and categorizing foods as low (<25%), medium (25–50%), and high (>50%) in whole grains. Foods and cereals in the database range from 0 to 97% whole grains (83).

Even if a comprehensive whole-grains database were developed, the diversity of whole grains and the products that include them make it difficult for consumers to accurately identify whole grains and whole-grain products. This can lead to inaccuracies in reporting whole-grain intakes in epidemiological studies and free-living intervention studies. The identification of whole-grain biomarkers that would independently reflect intake of whole grains would reduce the measurement errors known to occur with self-reported dietary records.

The development of a strategic research agenda is an important step in bringing together global research efforts, both epidemiological and intervention, to close existing knowledge gaps regarding whole grains and health. To be successful, strategic risk reduction requires focus and cooperation on areas of mutual and international interest along the entire whole-grains supply chain, from field to fork.

**Different whole grains = different health outcomes?** Most epidemiological studies have been conducted in populations that consume 60–90% of whole grains as wheat; thus, it is easy to assume that the observed reduction in disease risk is attributable to whole wheat. Other whole grains are just as likely to provide health benefits, but carrying out epidemiological studies on the health effects of individual whole grains, such as quinoa, barley, or rye, is difficult, because they are much less commonly consumed and, as with all whole grains, are consumed as part of a mixed diet. Although the findings of intervention studies on the health effects of individual whole grains would be of basic scientific interest, a consistent message needs to be translated to consumers. Demonstrating health benefits of individual grains would shed light on the variety of whole grains available, but the message to consumers should remain the same: eat more whole

grains as recommended by the 2010 Dietary Guidelines Advisory Committee and 2010 DGA.

Several studies have demonstrated, e.g., that whole-grain oats reduce both total and LDL cholesterol concentrations, accepted risk factors or biomarkers for CVD (84–88). In 1997, the U.S. FDA approved a health claim specific for  $\beta$ -glucan-soluble fiber from oats and barley for reducing plasma cholesterol concentrations and the risk of heart disease, the only such grain-specific health claim. In 2004, the United Kingdom Joint Health Claims Initiative allowed a similar health claim (89). Health Canada approved a similar claim in 2010 as well (90) and the European Food Safety Authority followed suit in 2011 (91). A recent review examined studies published during the previous 13 y and concluded that oat consumption is associated with an average 5 and 7% reduction in total and LDL cholesterol, respectively (89). Although consumption of other grains may not result in the same degree of lipid lowering, a variety of whole grains may yield the greatest overall health benefit, potentially due to their synergistic effects. Focusing on dietary patterns that include a variety of whole grains might be the more pertinent approach that would apply to real-world diets and outcomes.

#### **Holistic vs. reductionist approach to whole-grain research.**

Despite the rapidly growing evidence of a positive association between whole-grain consumption and long-term health, a research gap exists between observational studies and the elucidation of the mechanisms involved, which in some cases remain speculative (74). However, a synergistic effect of the many bioactive compounds present in whole grains is assumed (92). The most important groups of the whole-grain phytochemicals are phenolics [phenolic acids, alkylresorcinols (ARs), and flavonoids], carotenoids, vitamin E,  $\gamma$ -oryzanol, dietary fiber, and  $\beta$ -glucan (92). These compounds are unevenly distributed within the whole grain, primarily in the bran and germ fractions, and the distribution varies according to the type of grain (74).

Typically, the study of the health effects associated with whole grains takes either a reductionist approach, in which it is assumed that the dynamics of consuming whole grains can be understood by studying the properties of its parts, or a holistic approach, in which the dynamics can be understood only by examining the system as a whole, relying on the fundamental interconnectedness of biological systems. For whole grains, a reductionist approach would focus on the effects of fiber, lignans, phenolic acids, or phytosterols, e.g., in isolated systems. The concentration of individual bioactive compounds in whole grains is often low, perhaps below the threshold for any significant or lasting physiological effects to occur, even though long-term chronic intake of low concentrations could potentially have a beneficial effect (74). The reductionist approach may obscure important interrelationships among whole-grain components when whole-grain foods are consumed as part of a mixed diet. The holistic approach examines the health effects in humans of consuming specific types or forms of whole grains as part of an overall diet, but it may make it difficult to elucidate the actions of individual compounds found in whole grains (93). Although each approach offers unique insights, inaccessible through the other, neither is without limitations.

There are likely any number of mechanisms associated with the potential health effects of whole-grain consumption, which may be mechanical, hormonal, antioxidative, antiinflammatory, anticarcinogenic, or enzymatic or involve cell signaling (74). In addition, not all grain types or grain particle sizes have the same metabolic effects. Different physical structures yield different

metabolic profiles. SCFA production in the colon, as monitored by fecal SCFAs, was found to vary greatly according to grain particle size, whether whole wheat or wheat bran (78,94,95). A finer particle size of the whole grain has been found to both increase (78) and decrease (94) selective bacterial fermentation in the colon. Observed effects will vary depending upon which health outcome or biomarker is measured.

Both the chemical composition and food structure must be considered when studying the health benefits of whole grains. Bioprocessing of wheat bran, e.g., affects colonic metabolism of the phenolic compounds it contains (96). Distribution of water and air in the cereal matrix also is a key phenomenon controlling mouthfeel, digestibility, and physiological responses.

Nutrigenomics, the study of the influence of dietary interventions on gene expression, protein synthesis, and metabolites in cells, body fluids, and tissues, is a holistic approach that holds tremendous potential for extending knowledge of the protective mechanisms associated with complex foods, such as whole grains (74). A primary objective of nutrigenomics is to detect and identify early metabolic disturbances that might lead to chronic diseases. Studying the effects of bioactive compounds in whole grains on gene expression, protein synthesis, and metabolites could make it possible to better characterize the metabolic pathways affected by consumption of whole grains (74). However, there remains a need to relate these findings to established and yet-to-be accepted biomarkers and to health outcomes.

Both reductionist and holistic studies will be needed to elucidate the health benefits associated with whole-grains consumption as well as the mechanisms behind those benefits.

## Consumer Barriers to Whole-Grains Consumption

As the knowledge base for the potential health benefits of whole-grains consumption expands, consumer barriers to the acceptance of whole-grain foods remain. Among the barriers to increased consumption are consumer taste preferences, the substitution of whole grains for existing ingredients and in meal patterns, price, availability, and convenience (97). A stealth approach to substituting more healthful ingredients for less healthful options has been advocated by some to change dietary behavior. In a study of elementary school students in a large suburban school district, whole-wheat white flour was partially substituted for refined wheat flour in pizza crust without negatively affecting consumption and whole-grains consumption increased by nearly a full serving among fifth and sixth graders (98). While encouraging whole-grains consumption, consumer education efforts need to place greater emphasis on the substitution of whole grains for refined grains rather than simply adding more whole grains, and therefore more calories, to the diet.

In the US, the message consumers generally receive is to purchase products that are 100% whole grain, display the whole-grain stamp (indicating 8 or 16 g/serving of whole grains) or the whole-grain health claim (indicating the food contains  $\geq 51\%$  whole grains by weight per RACC), or have whole grains listed as the first ingredient on the label. However, food products that contain lesser amounts of whole grains may make significant contributions to whole-grain intake and should not be discounted. Not taking those foods into account in dietary assessments can lead to underestimation of whole-grain consumption. The issue then becomes whether the message to take

into account foods containing lesser amounts of whole grains would be confusing to consumers and make it even more difficult for them to judge whether they are consuming enough whole grains. Furthermore, in addition to the whole-grain content of the product, it is also important that the overall nutritional profile of the product (calories, fat, sugar, sodium) be taken into consideration when making whole-grain product recommendations to avoid unintended consequences. Also, it is important to emphasize substitution of refined grain products with whole-grain products rather than addition to current dietary intake practices to maintain calorie balance. The 2010 Dietary Guidelines recommend that at least half of recommended total grain intake be whole grains. For many, that is  $\sim 3$  servings/d (3 ounce equivalents = 48 g). In general, a 1-ounce equivalent from the grains group would translate to 1 slice of bread, 1 cup of ready-to-eat cereal, or 1/2 cup of cooked rice, cooked pasta, or cooked cereal, 1 tortilla (6-inch diameter), or 1 pancake (5-inch diameter). Fewer than 5% of Americans consume this minimum recommended amount of whole grains. Although food products that contain  $< 8$  g/serving of whole grains still contribute to the whole grains recommendation, the magnitude of that contribution cannot be captured using traditional dietary assessment methods such as FFQs. An analysis of dietary intakes in the UK in 2000–2001 suggested that 73% of whole-grain intake came from foods with  $\geq 51\%$  whole grains, 17% came from foods with 25 to  $< 51\%$  whole grains, and the remaining 10% was from foods with  $< 25\%$  (9).

The summit endorsed the need to standardize serving sizes both in the US and internationally (RACC vs. MyPlate vs. 1-oz equivalents vs. g whole grains/100 g or per serving) as well as to standardize definitions for what constitutes a whole-grain food. As it now stands, there are whole-grain standards for public health communications and policy, for nutrition labeling, and for health claims linked to specific products. The situation is confusing for both consumers and health professionals. These vary greatly from country to country, indicating a need for establishing international standards. Internationally, a fair but incomplete agreement of the definition of whole grain as a raw material exists, although official definitions are available in only a few countries. For food products, the situation is much less consistent and compared with that for raw materials, fewer definitions and regulations exist.

A whole-grains stamp program developed by the Whole Grains Council in the US enables consumers to easily identify whole-grain products that contain either 8 or 16 g of whole grains per serving by the presence of a unique stamp on products. Although the use of the stamp is growing, it is not universal and consumers may be unaware of its meaning and not be actively seeking out products that display the stamp. It is currently used in 35 countries outside the United States, including Argentina, Canada, China, Colombia, France, Greece, Ireland, Mexico, Netherlands, New Zealand, Poland, Singapore, Taiwan, UAE, UK, and Venezuela. Approximately 15% of all products using the whole-grain stamp are found outside the United States (99).

Efforts are underway to increase consumer education as to the importance of consuming whole grains through targeted messaging based on the 2010 DGA. Another of the primary messages of the 2010 DGA is to reduce sodium intake to  $\leq 1500$  mg/d (1). Most of the sodium in the American diet comes from baked goods as well as most of the fiber, which was identified as a short-fall nutrient by the Dietary Guidelines (3). This presents a nutrition/taste conundrum, i.e., how to increase whole-grain and fiber consumption yet retain the familiar taste consumers



enjoy without simultaneously increasing sodium intake above recommended limits. To address this issue, new technologies are currently being developed to reduce the sodium content in bread without affecting flavor, product safety, or shelf-life. One such technology employs "inhomogeneous spatial distribution" of salt in the food matrix, which can achieve up to a 25% reduction in salt in bread without loss of flavor intensity or the addition of taste enhancers, aromas, or salt replacers (100).

Another obstacle to increasing whole-grains consumption is the avoidance of all grain products, which is a growing global phenomenon because of real or perceived gluten intolerance or celiac disease, an inflammatory state of the small intestine that occurs in genetically predisposed individuals. Projections are that U.S. sales of gluten-free foods and beverages will exceed \$5 billion by 2015 (101). Gluten is the seed storage protein found in the endosperm of wheat, barley, and rye. There is no cure for celiac disease, but the exclusion of all dietary gluten resolves symptoms and allows healing of the mucosal lining of the small intestine. Celiac disease has been described as the result of a collision of genes and diet, a genetically determined autoimmune disorder triggered by a dietary staple (102). The condition rarely affects minority groups, but has been estimated to affect 1% of non-Hispanic whites in the US and the incidence is on the rise. There has been a substantial, almost 5-fold increase in the true prevalence of celiac disease over the last 50 y, affecting all ages (103). In addition, an unknown percentage of individuals may have non-celiac gluten sensitivity, in which they experience gastrointestinal symptoms in response to eating gluten-containing foods. Although celiac disease can be readily detected by blood tests for IgA, tissue transglutaminase antibodies (tTGA) and confirmed by biopsy, most cases remain undetected (104). One study of >5000 German men and women found that individuals with elevated IgA anti-tTG antibodies had an increased risk of mortality, particularly due to cancer (105). A study of almost 7000 Finnish adults, however, found no increased risk of mortality among tTGA-positive individuals, but they had a greater tendency to die from lymphoma (106).

It is unclear whether the increase in celiac disease is the result of a true increase in prevalence or merely better testing that has resulted in increased detection. It has been suggested that the increase could be due to increased wheat consumption, changes in wheat processing, or alterations in wheat genetics, or it could be due to unrelated environmental factors. Whatever the root cause of the increase, reduced intake of whole-grain wheat products could result in a decreased intake of whole-grain foods and the accompanying fiber and nutrients. Although the incidence of celiac disease is on the rise, there is also a growing number of individuals who avoid grains in the unsubstantiated belief that they suffer from gluten intolerance, making it even more difficult to meet dietary recommendations for whole-grain intake.

Consistent definitions of what constitutes a whole-grain product, uniform identification of whole-grain products, including those that contain lesser amounts of whole grains, identification of standardized serving sizes, and collaborative consumer education efforts on avoidance of grain products are needed to overcome some of the existing barriers to increasing consumption of whole-grain products.

## Research Challenges Ahead

Although short-term studies are informative, long-term studies are needed for health benefit substantiation. Designing and funding long-term intervention studies to examine the associa-

tion of whole grains and health, however, is a formidable endeavor. Even if funding were readily available, challenges associated with implementation must be overcome, including the inability to blind participants to the presence of whole grains in an intervention, the lack of compliance among participants, the lack of a standardized database to assess whole-grains intake and analytical tests to measure whole-grain content of foods, the lack of reliable surrogate markers for whole-grains intake, and the need to elucidate methods for accurately assessing how whole-grain foods relate to surrogate health outcomes, such as cholesterol concentrations.

Plasma ARs and urinary AR metabolites are currently being investigated as potential biomarkers for intake of whole-grain wheat and rye. ARs are a group of phenolic lipids mainly found in the outer bran layer of whole grains, and blood concentrations are reflective of recent intake. The WHOLEheart study found that plasma ARs increased with increasing intake of whole grains and that plasma concentrations could be used to distinguish between low and high whole-grain consumers (107). Potential biomarkers also exist for oats (avenanthramides) and whole-grain rice ( $\gamma$ -oryzanol), but both may be problematic because of low concentrations in foods. Little is known about the metabolism of avenanthramides, and absorption of  $\gamma$ -oryzanol is thought to be low (108). No unique, affordable, and relevant compounds have yet been identified in other key food grains, including corn, which is one of the main sources of whole grains in the U.S. population. Corn contains carotenoids, which have proved to be reliable indicators of fruit and vegetable intake, but none are unique to corn.

A standardized classification of whole-grain foods and a comprehensive nutrient database would address some of the methodological issues associated with accurate estimation of whole-grains intake. It has been suggested that combining valid biomarkers found in blood and urine with self-reported intakes could provide unbiased estimates of diet-disease associations (109). In addition to providing a way to associate whole-grains intake with health benefits, valid biomarkers would provide surrogate measures for intakes in population-based studies when no accurate dietary records are available (107, 110); it could confirm adherence in intervention studies (45) and possibly identify noncompliers.

The particular amount of whole-grain foods needed to confer health benefits is unclear due to difficulties in accurately assessing whole-grains intake in population studies. A study is currently underway at Newcastle University, UK (111) to investigate possible biomarkers (known and yet to be validated) of whole-grains intake and to find if certain substances present in whole grains are absorbed in the gut and appear in the blood and urine (111).

Given the difficulties in gathering evidence from intervention studies, the question arises whether observational studies should be relied upon to determine health benefits of whole-grains consumption, but observational studies present obstacles of their own. Although the FDA has defined whole grains, there is still disagreement as to what constitutes a whole grain in studies. Outdated and incomplete food databases are commonly used in both dietary intervention and observational studies. The development of an accurate, reliable, and up-to-date nutrient database for whole grains and foods that contain whole grains, akin to the Harvard whole-grains database, would require cooperation among government agencies, academic researchers, horticulture and agriculture professionals, and the food industry (112). Differences in whole-grain food definitions and measurements of whole grains and an inability to account for consumption of

products that contain lesser amounts of whole grains can contribute to inconsistent findings in population studies. There has been tremendous growth in the number of whole-grain products in recent years and, as a result, earlier population studies with relatively low intakes of whole grains could be underestimating the potential health benefits from higher whole-grains consumption.

Further research is needed with large-scale longitudinal studies, measuring surrogate risk markers at multiple times, involving ethnic groups, children, adolescents, and senior adults. There is a need to adopt a common system for conducting intervention studies, including methodology for collecting samples and standardization of research diets and for defining what a whole-grain food is.

For research efforts to be successful, all parties must reach across borders and collaborate on ways to improve the understanding of the health benefits of whole grains. Within the European Union, the HEALTHGRAIN Forum, a joint programming and action effort of 19 countries and 58 research and business partners, is underway to: 1) establish a consensus regarding the health benefits of whole grains; 2) develop better analysis and descriptors of cereal-based foods; 3) develop technologies to preserve health components of whole grains; 4) improve food composition tables allowing for more precise consumption data; 5) improve observational data analysis allowing for statements on country- and grain-specific health interpretations; and 6) disseminate information on generally accepted health benefits (health professionals, governmental agencies, policymakers, and industries) and improve consumer communication that is supported by all EU stakeholders. The ultimate goal is to reduce confusion by establishing one vision for research and communication (113). It is clear that these multiple tasks cannot be covered by one single company, university, funding agency, or even one country.

In the future, study data may need to include information on the physical and chemical characteristics of the whole grain that can affect digestion, insulin and glucose response, and gastric motility; the precise amount consumed; and observed health benefits based on biomarkers and related clear study endpoints. A comprehensive whole-grains database that would accurately assess intake both in population and intervention studies would help achieve these goals.

## Whole-Grain Technological Challenges

Although studies investigating the association between consumption of whole grains and health outcomes are essential, research into the development of improved technologies for processing whole grains to create more palatable whole-grain food products that consumers will accept is equally important. However, barriers exist that the industry must first overcome before it can reach its full potential and facilitate the mandate of the 2010 U.S. Dietary Guidelines for consumers to consume more whole grains. Several considerations come into play when delivering whole grains to consumers, among them product quality, taste, serving size, availability, stability of the food, other ingredients required, processing, and, lastly, consumer acceptance. To increase consumer acceptance of whole grains, it is important to optimize the flavor, color, and texture of foods made with whole-grain ingredients. As with most food product categories, health aspects of a food have a lower priority in the consumer's mind than taste, convenience, or price (114). However, the formulation and processing of foods made with

whole grains differ from and can be more challenging than those made with refined grains.

Although the technology to create healthful, whole-grain foods exists, the higher costs of whole grains, as well as the challenges presented in developing products acceptable to the broad range of consumer tastes, have constrained the food industry and slowed progress toward creating a broader range of available whole-grain foods. Production processes and equipment would need to be tailored to increased production of whole-grain products, but it is difficult to make considerable, large-scale changes in processing facilities because of costs. In addition, challenges exist regarding the amount of whole grains that realistically can be incorporated into a food in order to qualify for the whole-grains stamp. It is much easier, e.g., to incorporate 8 g (1/2 serving) of whole grains into a cracker when the serving size is 30 g than when the serving size is only 15 g.

Crop breeders must also join in the discussion of whole grains and health. Modern wheat cultivars have been bred for high white-flour yield, disease resistance, and food quality attributes unrelated to health. Wheat is currently considered a commodity, which keeps costs down, but it also holds back development of more nutritious ingredients. If the industry were to shift its focus to wheat as an ingredient rather than a commodity, it would be more inclined to generate new varieties with improved nutritional profiles. This is evident from the Australian program, which has led to the introduction of a novel barley high in total dietary fiber and resistant starch. A high-resistant starch wheat is currently under development. Such changes, however, are complex and expensive; new product innovations can take several months to several years to develop and do not come with guarantees that they will appeal to consumers (115).

It is imperative that lines of communication be established from consumer to processor and from processor to breeder. The goal is to facilitate the targeted breeding of wheat for improved human health by integrating screening for known bioactives into the screening protocol; evaluating the effects of these compounds on mammalian metabolism through cell culture, animal, and clinical trials; and to link the effects to specific regions on the wheat genome that can be targeted by plant breeders. This type of communication is currently taking place within the global oat-breeding program, where breeders are focusing on developing high-fiber, high- $\beta$ -glucan, and low-fat varieties. The entire oat research community and stakeholders have come together collectively to support the project. It promises to transform the future of oats by giving oat breeders the ability to make marker-assisted selections, growers another crop option, millers greater oat availability, and consumers continued access to a safe, heart-healthy, whole-grain food product (116). Their efforts could serve as a template for developing new cultivars of wheat and other whole grains with combined health, agronomic, and technological benefits. Breeders could also benefit from input from nutritionists as to which breeding objectives are the most nutritionally relevant.

Enhanced communication must also take place among manufacturers and distributors along with key players in government, industry, and foodservice establishments. These discussions must factor in rising energy and food-related costs, the increasing incidence of chronic diseases among both children and adults, and escalating health care costs. Future research should examine ways to improve consumer communication and acceptance of whole-grain foods to improve the industry's path to innovative product development, while bearing in mind the implementation of nutrition policy and regulatory recommendations and restrictions (117).

As the industry moves forward in developing healthier, whole-grain foods, cost considerations cannot be ignored, but the products benefit no one if they fail to provide the taste profile consumers expect. If these issues were to be resolved and consumer demand for whole grains were to increase, breeders, growers, and processors must ensure that the supply is able to keep up with demand. A shift in the food supply would be essential to meet such an increase in consumer demand for foods that are healthful, affordable, and practical. All sectors of the supply chain must form a working partnership to make it happen.

The grains community has a long history of working with public health officials to enhance the food supply in response to nutrient needs. Flour enrichment and fortification have decreased public health problems related to B-vitamin and iron deficiencies and, more recently, neural tube defects. A unified commitment by all parties is needed to create a sustainable food environment that ensures that new grain-based foods will also meet consumers' demands for convenience and good taste. The inclusion of more whole grain should also emphasize a more healthful overall food profile, such as smaller portion size, less caloric density, and lower sodium, that more closely meets dietary guidance. For this to take place, it will be necessary to build multi-sector partnerships across the food supply chain and embrace "shared value," i.e., developing and delivering better-for-you grain-based foods to consumers that will contribute to the good of business and to the well-being of society.

Consumers have been the traditional focus of educational efforts regarding whole grains. However, all segments of the food delivery system, from science (theory) to consumers (practice) must be engaged in these efforts. This will require contributions from interdisciplinary members of the supply chain combined with a formal infrastructure for disseminating information, clearly stated goals, clarification of individual and group roles, and the establishment of criteria for levels of whole grains in foods determined by an inclusive process.

A gradual, upward shift in the amount of whole grains incorporated into foods could provide a viable process for increasing the availability of healthful, whole-grain foods for consumers, particularly for underserved populations. Additionally, this would allow the industry to rise to the challenge put forth by the 2010 Dietary Guidelines Advisory Committee to make the healthy choice the easy choice and set the stage for increased consumption of whole grains to be an integral component of the 2015 DGA.

Accommodating an increased demand for whole-grain foods will take time to accomplish and the industry must work together to make incremental changes throughout the supply chain to create more healthful food products and make them available to consumers. A 10- to 15-y time frame would permit all sectors involved to adapt to the changes. This is a unique opportunity for the grain industry to set an example for how to effectively and efficiently translate nutrition policy into healthy products on grocery shelves.

## Conclusion

The 2010 DGA clearly advocate increased consumption of whole grains for health. This is an incremental step in the promotion of whole-grain consumption to improve health status. The evidence of a positive role for whole grains in disease prevention continues to reinforce and solidify that recommendation, particularly with regard to prevention of CVD, but also

shows promise for preventing type 2 diabetes, reducing hypertension, and aiding in weight regulation. Evidence is also emerging for the role of whole grains in lowering the risk of colorectal cancer. A greater understanding of the role of whole grains in health brings greater complexity to the problem, but it also offers new avenues of research. Studies are currently underway to identify and validate biomarkers of whole-grains consumption, not only to verify and confirm compliance with research protocols, but to assess intake of whole grains among the population, when accurate dietary intake assessment data are not available. It is imperative that whole-grain foods are accurately and uniformly characterized in studies and that evidence of health benefits be evaluated using well-developed whole-grain dietary/nutrient databases. Establishing an internationally accepted definition for whole grain foods and a comprehensive whole-grains database would make comparative evaluations of studies from around the world feasible.

Gaining a common understanding of whole-grain definitions, dietary guidance and intake, consumer behaviors, how whole grains travel from field to fork, evaluating whole grains' health benefits with state-of-science methodology, and creating collective solutions for public health are imperative for the future. Researchers must continue to plan, seek funding for, and implement studies on whole grains and health to solidify the knowledge base and fill knowledge gaps that currently exist. These efforts would be most beneficial if coordinated and shared internationally.

A great deal of progress has been made in recent years, but more research is needed to elucidate how whole grains work in the context of a mixed diet. Long-term intervention trials would be the ideal approach for measuring the effect of whole-grains consumption on health but are unlikely given the financial and logistical hurdles they would entail. Although randomized, controlled trials are still considered the gold standard for measuring the effect of diet on health outcomes, it is important to recognize the strength of observational cohort studies that show positive associations of whole grains and health. The findings from observational studies provide a framework to generate hypothesis-driven research questions to be answered, but higher intakes than are usual among the population may be necessary to observe highly significant differences in health outcomes, especially problematic when studying healthy populations and disease prevention is the outcome studied.

Consumers cite color, price, texture, and taste as major reasons they do not choose whole-grain products. It is up to public health officials and the food industry, together with grain breeders, food scientists, nutritionists, and educators to develop and promote whole-grain foods that appeal to the consumer. One approach would be to substitute whole-grain flour for refined flour in small amounts to bring about a meaningful impact on whole-grain intake at the population level. The overwhelming majority of flour is milled to produce refined flour. For increased availability and promotion of whole-grain foods to be most effective, public health officials and policy-makers must understand that food companies will require a "transition period" to bring a large selection of better-for-you, whole-grain products to market, occurring in stages over an extended period of time. Both chemical composition and food structure must be considered in the development and processing of palatable, health-promoting grain foods. While research continues, it is important to encourage whole-grain consumption as an important part of improving diets of the population as a whole and to remain cognizant of the limits of adaptability of

the consumer palate and proceed with gradual transitions to increased whole-grain contents of popular and frequently consumed foods in the diet.

Effective, long-term, public-private partnerships are needed to reach across the globe to galvanize the whole-grains community and collaborate effectively in translating whole-grain science into strategies that increase the availability and affordability of healthier grain-based food products. A prerequisite of that is the need to build trust among diverse multidisciplinary professionals involved in the growing, producing, and marketing of whole-grain products and between the grain and public health communities.

A number of issues were raised at the summit that remained unresolved. Several present potential future research opportunities in the areas of health nutrition, food technology and planning future studies.

**Health and Nutrition Research.** One of the issues repeatedly raised at the summit was the need to better understand the benefits of the whole-grain package, not just its individual components. Studies will need to be conducted to elucidate the possible synergistic effects of the individual whole-grain components as well as the impact of whole-grain consumption on overall diet quality and to identify the minimum amount of whole grains that is likely to confer health benefits. As celiac disease and self-imposed gluten avoidance are becoming increasingly common, research is needed to determine if avoidance of all gluten-containing products negatively affects nutrient intake and nutritional status. Education about gluten sensitivity is essential to prevent consumers from unnecessarily rejecting potentially beneficial whole-grain products.

**Considerations for Health and Nutrition Research.** Before research can provide answers, there are several study design issues that must be addressed, such as whether short-term studies can provide a clear picture of the health benefits of whole grains consumed as part of a healthful diet over the long term. In addition, the optimal study design to demonstrate cause-and-effect relationships with whole grains is difficult, for many reasons, to conduct. The isolation and identification of biomarkers of whole grains to provide tools to consistently measure consumption and compliance in intervention studies is needed. Also needed is a comprehensive whole-grain nutrient database derived from collaborative efforts of researchers and industry. From a broader perspective, collaborative discussions are necessary among those in the research community regarding the benefits of a reductionist compared with a holistic approach when studying the health attributes of whole grains.

**Technology.** The point was raised at the meeting that there is a need for breeding programs that will result in whole grains with improved health attributes, i.e., higher concentrations of nutrients or phytochemicals. More effective approaches must be developed for the incorporation of whole grains into different food matrices without negatively affecting consumer acceptance.

All of these must be addressed via a strategic research agenda that occurs in stages.

Stage I could include the establishment of core working partnerships from all sectors and disciplines within the grain community, including consumer groups.

Stage II would be to identify gaps that exist in delivering more healthful whole-grain foods that are well accepted by consumers.

In Stage III, collaborative partners would work together to define potential areas of research and define targets for research along the whole-grain supply chain.

Stage IV could consist of helping researchers connect current issues related to efficacy, affordability, practicality, and desirability with whole-grain issues. And in the fifth and final stage, research would be conducted and the findings applied to the development and delivery of more healthful whole-grain foods into the marketplace.

It will take the cooperation and coordination of all sectors of the grain industry over an extended period of time to “get it right.” However, a well-planned strategic research agenda carefully designed to fill knowledge gaps and help inform dietary guidance, coupled with renewed efforts from the grain industry, from farm to fork, to develop more whole-grain products that meet consumers’ lifestyle and tastes, and combined with nutrition education efforts that encourage the consumption of whole grains will ultimately have far-reaching effects on global health.

### Acknowledgments

D.W. drafted the paper; N.M.M., C.J.S., J.d.V., S.S.J., L.A.M., J.-W.v.K., D.T., D.D, and L.F.M. organized the Whole Grains Summit 2012; and L.F.M. had primary responsibility for final content. All authors read and approved the final manuscript.

### Literature Cited

1. USDA and U.S. Department of Health and Human Services. Dietary Guidelines for Americans, 2010. 7th ed. Washington, DC: U.S. Government Printing Office; 2010.
2. USDA [cited 2012 Sep 10]. ChooseMyPlate.gov. Available from: [www.choosemyplate.gov](http://www.choosemyplate.gov).
3. USDA, Agricultural Research Service, Dietary Guidelines Advisory Committee. Report of the Dietary Guidelines Advisory Committee on the Dietary Guidelines for Americans, 2010, to the Secretary of Agriculture and the Secretary of Health and Human Services. Washington, DC: USDA; 2010.
4. O’Neil CE, Nicklas TA, Zhanovec M, Cho S. Whole-grain consumption is associated with diet quality and nutrient intake in adults: the National Health and Nutrition Examination Survey, 1999–2004. *J Am Diet Assoc.* 2010;110:1461–8.
5. Jensen MK, Koh-Banerjee P, Franz M, Sampson M, Gronboek M, Rimm EB. Whole grains, bran, and germ in relation to homocysteine and markers of glycemic control, lipids and inflammation. *Am J Clin Nutr.* 2006;83:275–83.
6. Kyrø C, Skeie G, Dragsted LO, Christensen J, Overvad K, Hallmans G, Johansson I, Lund E, Slimani N, Johnsen NF, et al. Intake of whole grains in Scandinavia is associated with healthy lifestyle, socio-economic and dietary factors. *Public Health Nutr.* 2011;14:1787–95.
7. Kyrø C, Skeie G, Dragsted LO, Christensen J, Overvad K, Hallmans G, Johansson I, Lund E, Slimani N, Johnsen NF, et al. Intake of whole grain in Scandinavia: intake, sources and compliance with new national recommendations. *Scand J Public Health.* 2012;40:76–84.
8. DTU Food: The National Food Institute (Denmark) Fuldkorn: definition og vidensgrundlag for anbefaling af fuldkornsindtag i Danmark (Whole-grain: definition and scientific background for recommendations) [cited 2012 Jun]. Available from: <http://www.fuldkorn.dk/files/Rapporter/Fuldkorn%20definition%20og%20vidensgrundlag.pdf>.
9. Thane CW, Jones AR, Stephen AM, Seal CJ, Jebb SA. Comparative whole-grain intake of British adults in 1986–7 and 2000–1. *Br J Nutr.* 2007;97:987–92.
10. O’Neil CE, Nicklas TA, Zhanovec M, Cho SS, Kleinman R. Consumption of whole grains is associated with improved diet quality and nutrient intake in children and adolescents: the National Health and Nutrition Examination Survey 1999–2004. *Public Health Nutr.* 2011;14:347–55.
11. American Dietetic Association. Nutrition and you. Trends 2011 survey [cited 2012 Sep 12]. Available from: [www.eatright.org/nutritiontrends](http://www.eatright.org/nutritiontrends).
12. Danaei G, Finucane MM, Lu Y, Singh GM, Cowan MJ, Paciorek CJ, Lin JK, Farzadfar F, Khang YH, et al. National, regional, and global



- trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet*. 2011;378:31–40.
13. Danaei G, Finucane MM, Lin JK, Singh GM, Paciorek CJ, Cowan MJ, Farzadfar F, Stevens GA, Lim SS, et al. National, regional and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet*. 2011;377:568–77.
  14. Finucane MM, Stevens GA, Cowan MJ, Danaei G, Lin JK, Paciorek CJ, Singh GM, Gutierrez HR, Lu Y, et al. National, regional and global trends in body-mass index since 1980: systematic analysis of examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet*. 2011;377:557–67.
  15. United Nations. High-level meeting on non-communicable diseases. United Nations; 2011 [cited 2012 Sep 10]. Available from: <http://www.un.org/en/ga/president/65/issues/ncdiseases.shtml>.
  16. United Nations. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. Sixty-Sixth Session of the General Assembly; 2011 Sep 17. p. 1–13.
  17. Jones JM, Engleson J. Whole grains: benefits and challenges. *Annu Rev Food Sci Technol*. 2010;1:19–40.
  18. American Association of Cereal Chemists International. Whole-grain definition. *Cereal Foods World*. 1996;45:79.
  19. FDA. Health claim notification for whole-grain foods; 1999 [cited 2012 Sep 10]. Available from: [www.fda.gov/Food/LabelingNutrition/Label-Claims/FDAModernizationActFDAMAClaims/ucm073639](http://www.fda.gov/Food/LabelingNutrition/Label-Claims/FDAModernizationActFDAMAClaims/ucm073639)
  20. Björck I, Östman E, Kristensen M, Anson NM, Price R, Haenen GRMM, Havenaar R, Knudsen KEB, Frid A, et al. Cereal grains for nutrition and health benefits: overview of results from in vitro, animal and human studies in the HEALTHGRAIN project. *Tr Fd Sc Tech*. 2012;25:87–100.
  21. USDA, Nutrition Evidence Library [cited 2012 Aug 31] Available from: <http://www.nutritionevidencelibrary.gov/>.
  22. Hauner H, Bechthold A, Boeing H, Bronstrup, Buyken A, et al. Evidence-based guideline of the German Nutrition Society: carbohydrate intake and prevention of nutrition-related diseases. *Ann Nutr Metab*. 2012;60 Suppl 1:1–58.
  23. WHO. Global status report on non-communicable diseases 2010. Geneva: WHO; 2011.
  24. Morris JN, Marr JW, Clayton DG. Diet and heart: a postscript. *BMJ*. 1977;2:1307–14.
  25. Fraser GE, Strahan TM, Sabate J, Beeson WL, Kissinger D. Effects of traditional coronary risk factors on rates of incident coronary events in a low-risk population. The Adventist Health Study. *Circulation*. 1992;86:406–13.
  26. Pietinen P, Rimm EB, Korhonen P, Hartman AM, Willett WC, Albanes D, et al. Intake of dietary fiber and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Circulation*. 1996;94:2720–7.
  27. Jacobs DR Jr, Meyer KA, Kushi LH, Folsom AR. Whole-grain intake may reduce the risk of ischemic heart disease death in postmenopausal women: The Iowa Women's Health Study. *Am J Clin Nutr*. 1998;68:248–57.
  28. Liu S, Stampfer MJ, Hu FB, Giovannucci E, Rimm E, Manson JE, Hennekens CH, Willett WC. Whole-grain consumption and risk of coronary heart disease: results from the Nurses' Health Study. *Am J Clin Nutr*. 1999;70:412–9.
  29. U.S. Department of Health and Human Services. U.S. FDA. Health claim notification for whole grains foods [cited 2012 Oct 31]. Available from: <http://www.fda.gov/Food/LabelingNutrition/Label-Claims/FDAModernizationActFDAMAClaims/ucm073639.htm>.
  30. de Munter JSL, Hu FB, Spiegelman D, Franz M, van Dam RM. Whole grain, bran, and germ intake and risk of type 2 diabetes: a prospective cohort study and systematic review. *PLoS Med*. 2007;4:e261.
  31. Lefevre M, Jonnalagadda S. Effect of whole grains on markers of subclinical inflammation. *Nutr Rev*. 2012;70:387–96.
  32. Mellen PB, Walsh TF, Herrington DM. Whole grain intake and cardiovascular disease: a meta-analysis. *Nutr Metab Cardiovasc Dis*. 2008;18:283–90.
  33. Gaskins AJ, Mumford SL, Rovner AJ, Zhang C, Chen L, Wactawski-Wende J, Perkins NJ, Schisterman EF, BioCycle Study Group. Whole grains are associated with serum concentrations of high sensitivity C-reactive protein among premenopausal women. *J Nutr*. 2010;140:1669–76.
  34. He M, van Dam RM, Rimm E, Hu FB, Qi L. Whole-grain, cereal fiber, bran, and germ intake and the risks of all-cause and cardiovascular disease-specific mortality among women with type 2 diabetes mellitus. *Circulation*. 2010;121:2162–8.
  35. Ye EQ, Chacko SA, Chou EL, Kugizaki M, Liu S. Greater whole-grain intake is associated with lower risk of type 2 diabetes, cardiovascular disease, and weight gain. *J Nutr*. 2012;142:1304–13.
  36. Wang L, Gaziano JM, Liu S, Manson JE, Buring JE, Sesso HD. Whole- and refined-grain intakes and risk of hypertension in women. *Am J Clin Nutr*. 2007;86:472–9.
  37. Flint AJ, Hu FB, Glynn RJ, Jensen MK, Franz M, Sampson L, Rimm EB. Whole grains and incident hypertension in men. *Am J Clin Nutr*. 2009;90:493–8.
  38. Steffen LM, Kroenke CH, Yu X, Pereira MA, Slattery ML, Van Horn L, Gross MD, Jacobs DR Jr. Associations of plant food, dairy product, and meat intakes with 15-y incidence of elevated blood pressure in young black and white adults: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Am J Clin Nutr*. 2005;82:1169–77.
  39. Tighe P, Duthie G, Vaughan N, Brittenden J, Simpson WG, Duthie S, Mutch W, Wahle K, Horgan G, et al. Effect of increased consumption of whole-grain foods on blood pressure and other cardiovascular risk markers in health middle-aged persons: a randomized controlled trial. *Am J Clin Nutr*. 2010;92:733–40.
  40. Bodinham CL, Hitchen KL, Youngman PJ, Frost G, Robertson MD. Short-term effects of whole-grain wheat on appetite and of intake in healthy adults: a pilot study. *Br J Nutr*. 2011;106:327–30.
  41. Kochar J, Gaziano JM, Djousse L. Breakfast cereals and risk of hypertension in the Physicians' Health Study I. *Clin Nutr*. 2012;31:89–92.
  42. Jonnalagadda SS, Harnack L, Liu RH, McKeown N, Seal C, Liu S, Fahey GC. Putting the whole grain puzzle together: health benefits associated with whole grains: summary of American Society for Nutrition 2010 Satellite Symposium. *J Nutr*. 2011;141:S1011–22.
  43. Brownlee IA, Moore C, Chatfield M, Richardson DP, Ashby P, Kuznesof SA, Jebb SA, Seal CJ. Markers of cardiovascular risk are not changes by increased whole-grain intake: the WHOLEheart study, a randomized, controlled dietary intervention. *Br J Nutr*. 2010;2010:125–34.
  44. McKeown NM, Jacobs DR. In defence of phytochemical-rich dietary patterns. *Br J Nutr*. 2010;104:1–3.
  45. Kristensen M, Toubro S, Jensen MG, Ross AB, Riboldi G, Petronio M, Bügel S, Tetens I, Astrup A. Whole grain compared with refined wheat decreases the percentage of body fat following a 12-week, energy-restricted dietary intervention in postmenopausal women. *J Nutr*. 2012;142:710–6.
  46. Katcher HI, Legro RS, Kunselman AR, Gillies PJ, Demers LM, Bagshaw DM, Kris-Etherton PM. The effects of a whole-grain-enriched hypocaloric diet on cardiovascular disease risk factors in men and women with metabolic syndrome. *Am J Clin Nutr*. 2008;87:79–90.
  47. Jang Y, Lee JH, Kim OY, Park HY, Lee SY. Consumption of whole grain and legume powder reduced insulin demand, lipid peroxidation, and plasma homocysteine concentrations in patients with coronary artery disease. *Arterioscler Thromb Basc Biol*. 2001;21:2065–71.
  48. Jacobs DR Jr, Pereira MA, Stumpf K, Pins JJ, Adlercreutz H. Whole grain food intake elevates serum enterolactone. *Br J Nutr*. 2002;88:111–6.
  49. Peterson J, Dwyer J, Adlercreutz H, Scalbert A, Jacques P, McCullough ML. Dietary lignans: physiology and potential for cardiovascular disease risk reduction. *Nutr Rev*. 2010;68:571–603.
  50. WHO. Obesity and overweight. Fact Sheet No 311, May 2012 [cited 2012 May 24]. Available from: [www.who.int/mediacentre/factsheets/fs311/en/index.html](http://www.who.int/mediacentre/factsheets/fs311/en/index.html).
  51. Giacco R, Della Pepa G, Luongo D, Riccardi G. Whole grain intake in relation to body weight: from epidemiological evidence to clinical trials. *Nutr Metab Cardiovasc Dis*. 2011;21:901–8.
  52. Topping D, Bird A, Toden S, Conion M, Noakes M, King R, Mann G, Li Z, Morell M. Resistant starch as a contributor to the health benefits of whole grains. In: Marquart L, Jacobs D, McIntosh G, Poutanen K, Reicks M, editors. *Whole grains and health*. Ames (IA): Blackwell Publishers; 2007; 219–28.

53. Koh-Banerjee P, Franz M, Sampson L, Liu S, Jacobs DR, Spiegelman D, Willett W, Rimm E. Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight gain among men. *Am J Clin Nutr.* 2004;80:1237–45.
54. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. *Am J Clin Nutr.* 2003;78:920–7.
55. Melanson KJ, Angelopoulos TJ, Nguyen VT, Martini M, Zukley L, Lowndes J, Dube TJ, Fiutem JJ, Yount BW, et al. Consumption of whole-grain cereals during weight loss: effects on dietary quality, dietary fiber, magnesium, vitamin B-6, and obesity. *J Am Diet Assoc.* 2006;106:1380–88.
56. Rave K, Roggen K, Dellweg S, Heise T, tom Kieck H. Improvement of insulin resistance with a whole-grain based dietary product: results of a randomized, controlled cross-over study in obese subjects with elevated fasting blood glucose. *Br J Nutr.* 2007;98:929–36.
57. Maki KC, Beiseigel JM, Jonnalagadda SS, Gugger CK, Reeves MS, Farmer MV, Kaden VN, Rains TM. Whole-grain ready-to-eat oat cereal, as part of a dietary program for weight loss, reduces low-density lipoprotein cholesterol in adults with overweight and obesity more than a dietary program including low-fiber control foods. *J Am Diet Assoc.* 2010;110:205–14.
58. McKeown NM, Troy LM, Jacques PF, Hoffmann U, O'Donnell CJ, Fox CS. Whole- and refined-grain intakes are differentially associated with abdominal visceral and subcutaneous adiposity in healthy adults: the Framingham Heart Study. *Am J Clin Nutr.* 2010;92:1165–71.
59. Zanovec M, O'Neil CE, Cho SS, Kleinman RE, Nicklas TA. Relationship between whole grain and fiber consumption and body weight measures among 6- to 18-year-olds. *J Pediatr.* 2010;157:578–83.
60. Hur IY, Reicks M. Relationship between whole-grain intake, chronic disease risk indicators, and weight status among adolescents in the National Health and Nutrition Examination Survey, 1999–2004. *J Acad Nutr Diet.* 2012;112:46–55.
61. Choumenkovitch SF, McKeown NM, Tovar A, Hyatt RR, Kraak VI, Hastings AV, Herzog JB, Economos CD. Whole grain consumption is inversely associated with BMI Z-score in rural school-aged children. *Public Health Nutr.* 2013;16:212–8.
62. International Diabetes Federation. *IDF Diabetes Atlas, 5th ed.* Brussels: International Diabetes Federation; 2011.
63. Pereira MA, Jacobs DR Jr, Pins JJ, Raatz SK, Gross MD, Slavin JL, Seaquist ER. Effect of whole grains on insulin sensitivity in overweight hyperinsulinemic adults. *Am J Clin Nutr.* 2002;75:848–55.
64. Lankinen M, Schwab U, Kolehmainen M, Paananen J, Poutanen K, Mykkänen H, Seppänen-Laakso T, Gylling H, Uusitupa M, et al. Whole grain products, fish and bilberries alter glucose and lipid metabolism in a randomized, controlled trial: The Sysdimet Study. *PLoS ONE.* 2011;6:e22646.
65. de Mello VD, Schwab U, Kolehmainen M, Koenig W, Siloaho M, Poutanen K, Mykkänen H, Uusitupa M. A diet high in fatty fish, bilberries and wholegrain products improves markers of endothelial function and inflammation in individuals with impaired glucose metabolism in a randomised controlled trial: the Sysdimet study. *Diabetologia.* 2011;54:2755–67.
66. American Cancer Society. *Global cancer facts and figures.* 2nd ed. Atlanta: American Cancer Society; 2011.
67. McCullough ML, Robertson AS, Chao A, Jacobs EJ, Stampfer MJ, Jacobs DR, Diver WR, Calle EE, Thun MJ. A prospective study of whole grains, fruits, vegetables and colon cancer risk. *Cancer Causes Control.* 2003;14:959–70.
68. Larsson SC, Giovannucci E, Bergkvist L, Wolk A. Whole grain consumption and risk of colorectal cancer: a population-based cohort of 60,000 women. *Br J Cancer.* 2005;92:1803–7.
69. Schatzkin A, Mouw T, Park Y, Subar AF, Kipnis V, Hollenbeck A, Leitzmann MF, Thompson FE. Dietary fiber and whole-grain consumption in relation to colorectal cancer in the NIH-AARP Diet and Health Study. *Am J Clin Nutr.* 2007;85:1353–60.
70. Egeberg R, Olsen A, Loft S, Christensen J, Johnsen NF, Overvad K, Tjønneland A. Intake of wholegrain products and risk of colorectal cancers in the Diet, Cancer and Health cohort study. *Br J Cancer.* 2010;103:730–4.
71. Aune D, Chan DS, Lau R, Vieira R, Greenwood DC, Kampman E, Norat T. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ.* 2011;343:d6617.
72. Fung TT, Hu FB, Wu K, Chiuve SE, Fuchs CS, Giovannucci E. The Mediterranean and Dietary Approaches to Stop Hypertension (DASH) diets and colorectal cancer. *Am J Clin Nutr.* 2010;92:1429–35.
73. Conlon MA, Kerr C, McSweeney CS, Dunne RA, Shaw JM, Kang S, Bird AR, Morell MK, Lockett TJ, Molloy PL, et al. Resistant starches protect against colonic DNA damage and alter microbiota and gene expression in rats fed a Western diet. *J Nutr.* 2012;142:832–40.
74. Fardet A. New hypotheses for the health-protective mechanisms of whole-grain cereals: what is beyond fibre? *Nutr Res Rev.* 2010;23:65–134.
75. Gibson GR, Probert HM, Loo JV, Rastall RA, Roberfroid MB. Dietary modulation of the human colonic microbiota: updating the concept of prebiotics. *Nutr Res Rev.* 2004;17:259–75.
76. Costabile A, Klinder A, Fava F, Napolitano A, Fogliano V, Leonard C, Gibson GR, Tuohy KM. Whole-grain wheat breakfast cereal has a prebiotic effect on the human gut microbiota: a double-blind, placebo-controlled crossover study. *Br J Nutr.* 2008;99:110–20.
77. Carvalho-Wells AL, Helmolz K, Nodet C, Moizer C, Leonard C, McKeivith B, Thielecke F, Jackson KG, Tuohy KM. Determination of the in vivo prebiotic potential of a maize-based whole grain breakfast cereal: a human study. *Br J Nutr.* 2010;104:1353–6.
78. Connolly ML, Lovegrove JA, Tuohy KM. In vitro evaluation of the microbiota modulation abilities of different sized whole oat grain flakes. *Anaerobe.* 2010;16:483–8.
79. Hooda S, Boler BM, Seroo MC, Brulc JM, Staeger MA, Boileau TW, Dowd SE, Fahey GC Jr, Swanson KS. 454 pyrosequencing reveals a shift in fecal microbiota of healthy adult men consuming polydextrose or soluble corn fiber. *J Nutr.* 2012;142:1259–65.
80. Holmes E, Li JV, Athanasiou T, Ashrafiyan H, Nicholson JK. Understanding the role of gut microbiome: host metabolic signal disruption in health and disease. *Trends Microbiol.* 2011;19:349–59.
81. Sijtsma FP, Meyer KA, Steffen LM, Shikany JM, Van Horn L, Harnack L, Kromhout D, Jacobs DR Jr. Longitudinal trends in diet and effects of sex, race, and education on dietary quality score change: the Coronary Artery Risk Development in Young Adults study. *Am J Clin Nutr.* 2012;95:580–6.
82. PREvención con Dieta MEDiterránea (PREDIMED) Study [cited 2012 Sep 1]. Available from: <http://predimed.onmedic.net/eng/Home/tabid/357/Default.aspx>.
83. Franz M, Sampson L. Challenges in developing a whole grain database: definitions, methods and quantification. *J Food Comp Anal.* 2006;S38–44.
84. Van Horn LV, Liu K, Parker D, Emidy L, Liao YL, Pan WH, Giumetti D, Hewitt J, Stamler J. Serum lipid response to oat product intake with a fat-modified diet. *J Am Diet Assoc.* 1986;86:759–64.
85. Johnston L, Reynolds HR, Patz M, Hunninghake DB, Schulz K, Westereng B. Cholesterol-lowering benefits of a whole grain oat ready-to-eat cereal. *Nutr Clin Care.* 1998;1:6–12.
86. Van Horn L, Emidy LA, Liu KA, Liao YL, Ballew C, King J, Stamler J. Serum lipid response to a fat-modified, oatmeal-enhanced diet. *Prev Med.* 1988;17:377–86.
87. Reynolds H, Lindeke E, Hunninghake D. Effect of oat bran on serum lipids. *J Am Diet Assoc.* 1989;89 Suppl 9:A112.
88. Van Horn L, Moag-Stahlberg A, Liu KA, Ballew C, Ruth K, Hughes R, Stamler J. Effects on serum lipids of adding instant oats to usual American diets. *Am J Public Health.* 1991;81:183–8.
89. Othman RA, Moghadasian MH, Jones PJ. Cholesterol-lowering effects of oat  $\beta$ -glucan. *Nutr Rev.* 2011;69:299–309.
90. Health Canada. Oat products and blood cholesterol lowering. Summary of assessment of a health claim about oat products and blood cholesterol lowering. Bureau of Nutritional Sciences, Food Directorate, Health Products and Food Branch. November 2010 [cited 2012 Sep 10]. Available from: [http://www.nithriver.ca/oat\\_avoine-eng.pdf](http://www.nithriver.ca/oat_avoine-eng.pdf).
91. EFSA Panel on Dietetic Products, Nutrition and Allergies. Scientific opinion on the substantiation of a health claim related to barley beta-glucan and lowering of blood cholesterol and reduced risk of (coronary) heart disease pursuant to Article 14 of Regulation (EC) No 1924/2006. *EFSA J.* 2001;9:24770.
92. Liu RH. Whole grain phytochemicals and health. *J Cereal Sci.* 2007;46:207–19.

93. Fang FC, Casadevall A, Fang FC, Casadevall A. Reductionistic and holistic science. *Infect Immun*. 2011;79:1401–4.
94. Jenkins DJA, Kendall CWC, Uksan V, Augustin L, Li YM, Lee B, Mehling CC, Parker T, Faulkner D, et al. The effect of wheat bran particle size on laxation and colonic fermentation. *J Am Coll Nutr*. 1999;18:339–45.
95. Stewart ML, Slavin JL. Particle size and fraction of wheat bran influence short-chain fatty acid production in vitro. *Br J Nutr*. 2009;102:1404–7.
96. Anson NM, Selinheimo E, Havenaar R, Aur AM, Mattila I, Lehtinen P, Bast A, Poutanen K, Haenen GR. Bioprocessing of wheat bran improves in vitro bioaccessibility and colonic metabolism of phenolic compounds. *J Agric Food Chem*. 2009;57:6148–55.
97. Kuznesof S, Brownlee IA, Moore C, Richardson DP, Jebb SA, Seal CJ. WHOLEheart study participant acceptance of wholegrain foods. *Appetite*. 2012;59:187–93.
98. Chan H, Burgess-Champoux T, Reicks M, Vickers Z, Marquart L. White whole wheat flour is partially substituted for refined wheat flour in pizza crust in school meals. *J Child Nutr Manag*. 2008;32 [cited 2012 Sep 10]. Available from: <http://www.schoolnutrition.org/Content.aspx?id=8334>.
99. The Whole Grains Council. Whole Grain Stamp [cited 2012 Sep 15]. Available from: [www.wholegrainscouncil.org](http://www.wholegrainscouncil.org).
100. Noort MWJ, Bult JHF, Stieer M, Hamer RJ. Saltiness enhancement in bread by inhomogeneous spatial distribution of sodium chloride. *J Cereal Chem*. 2011;141:2249–55.
101. Packaged Facts. Gluten-free foods and beverages in the U.S. 3rd ed, February 1, 2011 [cited 2012 Sep 10]. Available from: <http://www.packagedfacts.com/Gluten-Free-Foods-2710664/>.
102. Cordain L. Cereal grains: humanity's double-edged sword in evolutionary aspects of nutrition and health. *Diet, exercise, genetics and chronic disease*. *World Rev Nutr Diet*; 1999;84:19–73.
103. Rubio-Tapia A, Kyle RA, Kaplan EL, Johnson DR, Page W, Erdtmann F, Brantner TL, Kim WR, Phelps TK, Lahr BD, et al. Increased prevalence and mortality in undiagnosed celiac disease. *Gastroenterology*. 2009;137:88–93.
104. Rubio-Tapia A, Ludvigsson JF, Brantner TL, Murray JA, Everhart JE. The prevalence of celiac disease in the United States. *Am J Gastroenterol*. 2012;107:1538–44.
105. Metzger MH, Heier M, Maki M, Bravi E, Schneider A, Löwel H, Illig T, Schuppan D, Wichmann HE. Mortality excess in individuals with elevated IgA anti-transglutaminase antibodies: the KORA/MONICA Augsburg cohort study 1989–1998. *Eur J Epidemiol*. 2006;21:359–65.
106. Lohi S, Maki M, Rissanen H, Knekt P, Reunanen A, Kaukinen K. Prognosis of unrecognized coeliac disease as regards mortality: a population-based cohort study. *Ann Med*. 2009;41:508–15.
107. Ross AB, Bourgeois A, Macharia HN, Kochhar S, Jebb SA, Brownlee IA, Seal CJ. Plasma alkylresorcinols as a biomarker of whole-grain food consumption in a large population: results from the WHOLE-heart Intervention Study. *Am J Clin Nutr*. 2012;95:204–11.
108. Ross AB. Present status and perspectives on the use of alkylresorcinols as biomarkers of wholegrain wheat and rye intake. *J Nutr Metab*. 2012;2012:462967.
109. Freedman LS, Midthune D, Carroll RJ, Tasevska M, Schatzkin A, Mares J, Tinker L, Potischman N, Kipnis V. Using regression calibration equations that combine self-reported intake and biomarker measures to obtain unbiased estimates and more powerful tests of dietary association. *Am J Epidemiol*. 2011;174:1238–45.
110. Ma J, Ross AB, Shea MK, Bruce SJ, Jacques PF, Saltzman E, Lichtenstein AH, Booth SL, McKeown NM. Plasma alkylresorcinols, biomarkers of whole grain intake, are related to lower BMI in older adults. *J Nutr*. 2012;142:1859–64.
111. Halder S, Bal W, Brandt K, Seal C. Effect of consumption of either whole grain or rye as the sole whole grain source on plasma lipid profiles in healthy volunteers (the GrainMark Study). Presented at Whole Grains Summit 2009. GrainMark Study [cited 2012 Sep 10]. Available from: <http://www.ncl.ac.uk/afrd/research/project/2287>.
112. Jensen MK, Koh-Banerjee P, Hu FB, Franz M, Sampson L, Gronbark M. Intakes of whole grains, bran, and germ and the risk of coronary heart disease in men. *Am J Clin Nutr*. 2004;80:1492–9.
113. Health Grain Forum [cited 2012 Aug 30]. Available from: [www.healthgrain.org](http://www.healthgrain.org).
114. Rowe S, Alexander N, Almeida N, Black R, Burns R, Bush L, Crawford P, Keim N, Kris-Etherton P, et al. Food science challenge: translating the Dietary Guidelines for Americans to bring about real behavior change. *J Food Sci*. 2011;76:R29–37.
115. Institute of Medicine. Leveraging Food Technology for Obesity Prevention and Reduction Efforts Workshop summary. Institute of Medicine (US) Food Forum. Washington, DC: National Academies Press; 2011.
116. North American Millers Association [cited 2012 Oct 25]. Available from: [http://www.namamillers.org/PR\\_Oat\\_Research\\_10\\_14\\_09.html](http://www.namamillers.org/PR_Oat_Research_10_14_09.html).
117. Hesse D, Braun C, Dostal A, Jeffery R, Marquart L. Barriers and opportunities related to whole grain foods in Minnesota school foodservice. *J Child Nutr Manag*. 2009;33 [cited 2012 Sep 10]. Available from: <http://www.schoolnutrition.org/Content.aspx?id=12511>.
118. van de Vijver LP, van den Bosch LM, van den Brandt PA, Goldbohm RA. Whole grain consumption, dietary fiber intake and body mass index in the Netherlands cohort study. *Eur J Clin Nutr*. 2009;63:31–8.
119. USDA, Agricultural Research Service. USDA National Nutrient Database for Standard Reference. Release 24. Nutrient Data Laboratory Home Page; 2011 [cited 2012 Sep 10]. Available from: <http://www.ars.usda.gov/ba/bhnrc/dl>.