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Supplement: Putting the Whole Grain Puzzle Together: Health Benefits Associated with Whole Grain—Summary of American Society for Nutrition 2010 Satellite Symposium

Putting the Whole Grain Puzzle Together: Health Benefits Associated with Whole Grains—Summary of American Society for Nutrition 2010 Satellite Symposium[1-3]

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Abstract

The symposium "Putting the Whole Grain Puzzle Together: Health Benefits Associated with Whole Grains" sponsored by the ASN brought together researchers to review the evidence regarding the health benefits associated with whole grains. Current scientific evidence indicates that whole grains play an important role in lowering the risk of chronic diseases, such as coronary heart disease, diabetes, and cancer, and also contribute to body weight management and gastrointestinal health. The essential macro- and micronutrients, along with the phytonutrients present in whole grains, synergistically contribute to their beneficial effects. Current evidence lends credence to the recommendations to incorporate whole grain foods into a healthy diet and lifestyle program. The symposium also highlighted the need for further research to examine the role of whole grain foods in disease prevention and management to gain a better understanding of their mechanisms of action. J. Nutr. 141: 1011S–1022S, 2011.

Introduction

On April 23, 2010, at the Experimental Biology Annual Meeting, the ASN, through an unrestricted education grant from the General Mills Bell Institute of Health and Nutrition, sponsored a satellite symposium on "Putting the Whole Grain Puzzle Together: Health Benefits Associated with Whole Grain." The symposium brought together researchers who reviewed the evidence associated with whole grain health benefits in the areas of: whole grain phytonutrients, weight management, cardiovascular disease (CVD),[11] diabetes, digestive health, and ways to help improve whole grain dietary intake assessment. This paper briefly summarizes the evidence reviewed during the symposium and the recommendations for future research on the health benefits of whole grains.

Whole grains

Whole grains are defined by the American Association of Cereal Chemists International and the FDA as consisting of the "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 (1,2)." Whole grain foods that undergo processing and reconstitution must deliver the same proportion of bran, germ, and endosperm as that of the original grain to be considered whole grains (1,2). The outer bran layer is composed of nondigestible,

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[11] Abbreviations used: CHD, coronary heart disease; CRP, C-reactive protein; CVD, cardiovascular disease; NCC, Nutrition Coordinating Center; RS, resistant starch; TE, Trolox equivalent.

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mainly insoluble, poorly fermentable carbohydrates (such as cellulose, hemicelluloses, arabinoxylan), and the inner germ and starchy endosperm contain viscous soluble fibers, fermentable oligosaccharides, resistant starch (RS), lignans, vitamins, minerals, polyphenols, oils, and other phytonutrients (3). During the refining of whole grains into white flour, the outer bran and inner germ layers are removed and the remaining endosperm is processed into flour. Thus, compared with refined grains, whole grains are inherently richer in dietary fiber, containing ~80% more dietary fiber than refined grains (3,4). Furthermore, as a consequence of the refining process, there are substantial losses in essential minerals, vitamins, and phytonutrients (3,4).

The 2005 Dietary Guidelines for Americans recommend that individuals should "consume 3 or more ounce-equivalents of whole grain products per day, with the rest of the recommended grains coming from enriched or whole-grain products. In general, at least half of the grains should come from whole grains (5)." The 2010 Dietary Guidelines for Americans continues to support this guidance (6).

Despite the current dietary guidelines recommending that individuals consume at least one-half of all their grains as whole grains (i.e. 3 servings/d; 1 serving = 16 g), dietary intake data from the Continuing Survey of Food Intakes and the NHANES indicate that the average whole grain intake is 1 serving/d, with 95% of Americans not meeting their whole grain daily intake recommendations (7,8). There is some evidence that, since the 2005 Dietary Guidelines for Americans, consumers have increased purchases of whole grain foods, particularly ready-to-eat breakfast cereals, breads, and pasta, which may in part be due to more products with whole grains being available on supermarket shelves (9).

In 2001–2002, the leading food sources of whole grains in the American diet were ready-to-eat cereal (28.7%), yeast breads (25.3%), hot cereals (13.7%), popcorn (12.4%), and crackers (6.4%), with these food categories accounting for close to 90% of all whole grains consumed (10). The most common types of whole grains in the American diet are wheat, corn, oats, barley, and rice, with wheat being the most prominent grain consumed on a daily basis. **Table 1** shows the common whole grains and examples of food products and **Table 2** shows the macronutrient composition of the common grains (4).

TABLE 1 Common whole grains and examples of whole grains food products

True cereals (common names)	Pseudo cereals
Wheat	Amaranth
Oat	Buckwheat
Barley	Quinoa
Brown rice	
Maize (corn)	
Rye	
Millets	
Sorghum	
Teff	
Triticale	
Examples of common whole grain food products	
Whole wheat flour	Whole grain (wheat) pasta
Whole wheat bread	Whole grain (wheat, corn, etc.) tortilla
Rolled oats, oatmeal	Brown rice
Popcorn	Baked goods (e.g. whole wheat blueberry muffin, whole wheat bread)
Rye bread	Whole grain ready-to-eat breakfast cereal
	Whole grain snacks (crackers, bars, etc.)

TABLE 2 Macronutrient composition of whole grains[1]

Grain	Energy	Total carbohydrate	Protein	Total fat	Total dietary fiber
	kJ /100 g		*g/100 g*		
Wheat, soft white	1421	75.4	10.7	1.99	12.7
Oat	1626	66.3	16.89	6.90	10.6
Barley, hulled	1480	73.5	12.48	2.3	17.3
Rice, brown, long-grain	1547	77.2	7.9	2.9	3.5
Corn, yellow	1526	74.3	9.4	4.7	7.3
Rye	1413	75.9	10.3	1.6	15.1
Millets	1580	72.8	11.0	4.2	8.5
Sorghum	1413	74.6	11.3	3.3	6.3
Teff	1534	73.1	13.3	2.4	8.0
Triticale	1404	72.1	13.0	2.1	Not available

[1] Data are from (4).

Whole grain foods can contain the intact whole grain or be reconstituted in that they have components of the whole grains recombined to the relative proportion as naturally occurring in the grain kernel (1,2). The majority of products found on retail store shelves would be considered reconstituted whole grain products (11).

Whole grain dietary intake assessment

Estimation of an individual's whole grain intake can be obtained in a variety of ways, such as 24-h dietary intake recalls, food records, and FFQ, with the latter being the most common method used in epidemiological studies. In all of these dietary intake assessment methods, the definition of whole grain food is important to clearly understand. Definitions of whole grain foods have varied from study to study and nutrient intake database to database. In early studies, whole grain foods included whole grain breakfast cereals (containing ≥25% of whole grain content), dark bread, brown rice, oatmeal, and other specific individual foods such as wild rice, whole wheat crackers, and bran muffins (see **Tables 3** and **4** for individual studies). In addition, added bran and added germ were included in the whole grain category. Thus, based on the definition of what is considered a whole grain food, whole grain intake can be either under- or overestimated. This calls for the need for standardizing dietary intake assessment methods to better quantify whole grain intake.

There are a number of methodological challenges to developing a standardized approach to accurately quantify consumption of whole grain foods. The greatest challenge may be coping with foods that contain a combination of whole and nonwhole grain ingredients. It is a methodological issue that must be addressed, because a growing number of partial whole grain foods appear to be entering the marketplace. The proliferation of partial whole grain foods is likely occurring for various reasons, such as technical feasibility, shelf-life stability, taste, acceptance, and cost. For example, with respect to taste and acceptance, Sadeghi and Marquart (12) showed that graham crackers that were partially whole grains (5 g/serving) had a higher rate of acceptance by elementary school children compared with 100% whole grain graham crackers (26 g/serving).

TABLE 3 Cross-sectional and prospective evidence in adults demonstrating higher whole grain intake is associated with lower BMI and smaller waist circumference

Cohort/reference	Higher whole grain intake is associated with		
	Lower BMI	Smaller waist circumference	Less weight gain
Cross-sectional studies			
Framingham Offspring Study (25)	X[1]	—[2]	—
Nurses' Health Study (26)	X	—	—
Health Professionals Follow-up Study (27)	X	—	—
Physicians' Health Study (28)	X	—	—
Healthy community living older adults (29)	X	—	—
Multi-Ethnic Study of Atherosclerosis (30)	X	—	—
Baltimore Longitudinal Study of Aging (31)	X	X	—
College students enrolled in a nutrition course (32)	X	—	—
National Health and Nutrition Examination Survey 1999–2000 (8)	X	X	—
Free-living adults (33)	X	—	—
Tehran Lipid and Glucose Study (34, 35)	—	X	—
Netherlands Cohort Study (36)	X	—	—
Dietary and Nutritional Survey of British Adults (37)	NS[3]	NS	—
Prospective studies			
Nurses' Health Study (26)	—	—	X
Health Professionals Follow-up Study (27)	—	—	X

[1] X, Significant association found, $P < 0.05$.
[2] —, Not tested in the study.
[3] NS, No significant association found, $P \geq 0.05$.

Foods that are partially whole grains are methodologically problematic, because often the relative proportion of whole and nonwhole grain ingredients in the product is unknown and is proprietary formulation information of the food manufacturers. What is known about these products is the rank order of grain ingredients as provided on the FDA required ingredient statement on product packaging. From the ingredient statement, clues are provided as to the relative proportion of whole and nonwhole grain ingredients. As an example, if the first ingredient listed on the product packaging of a cracked wheat bread product is enriched wheat flour and the second and only other grain ingredient listed is whole wheat flour, it may be surmised that the product contains more nonwhole grain than whole grain ingredients. What is unknown is the exact relative proportion. In

TABLE 4 Cross-sectional and prospective evidence on the association between whole grain intake and CVD

Cohort/reference	Higher whole grain intake is associated with lower					
	CVD mortality	CHD/CAD risk/mortality	Ischemic stroke	Nonfatal MI	Blood pressure/hypertension	Blood lipids
Cross-sectional studies						
MESA (30)	—[1]	—	—	—	NS[2]	NS
BLSA (31)	—	—	—	—	NS	X[3]
HPFS & NHS II (51)	—	—	—	—		X
Elderly population in Boston (29)	—	—	—	—	NS	NS
Tehran Lipid and Glucose Study (34, 35)	—	—	—	—	X	X
Framingham Offspring Study (25)	—	—	—	—	NS	X
Yi Migrant Study (52)	—	—	—	—	X	X
Prospective studies						
HPFS (53)	—	—	NS	—	X	—
NHS (54)	—	—	NS	—	X	—
CARDIA Study (55)	—	—	—	—	X	—
HPFS (56)	—	X	—	—	—	—
Physician Health Study (57)	X	—	—	—	—	—
Atherosclerosis Risk in Communities Study (ARIC) (58)	—	X	NS	—	—	—
NHS (59)	—	—	NS	—	—	—
Iowa Women's Health Study (60)	X	X		—	—	—
NHS (61)	—	X	—		—	—
Adventist Health Study (62)	—	X	—	X	—	—

[1] —, Not tested in the study.
[2] NS, No significant association found, $P \geq 0.05$.
[3] X, Significant association found, $P < 0.05$.

this example, the proportion of grains in the cracked wheat bread that is whole grain could be anywhere from 49 to 1%, thus qualifying it to be considered a whole grain food.

In consideration of the lack of detailed information about the quantity of whole and nonwhole grain ingredients in many partial whole grain food products, there are several approaches that may be considered for quantifying the contribution of partial whole grain foods to whole grain intake. One potential simplistic option is to count a food as whole grain only if all the grain ingredients are whole, but if the total grain amount in the food is minimal, then it could result in an overestimation of whole grain contribution. Conversely, a rule could be established whereby a food would be considered a whole grain if it contained 1 or more whole grain ingredients (any whole grain). The primary shortcoming of this type of approach is that whole grain intake is apt to be underestimated or overestimated, with the misclassification particularly acute among those who regularly consume partial whole grain foods.

Another more complex option is to consider a food as whole grain if the first ingredient is whole grain, partial whole grain if whole grains are not the first ingredient, and not a whole grain food if there are no whole grain ingredients (13). Although this option tries to account for the varying levels of whole grain composition of food products, it is hard to interpret and quantify the partial whole grain classification. For example, using this approach, a summary measure of servings of whole grains cannot be calculated without assumptions being made about the relative contribution of partial whole grain servings.

A more complex but potentially more accurate method of determining whole grain intake is to estimate the relative proportion of whole grain and nonwhole grains components, which is the approach used by the MyPyramid equivalent database (11). This approach relies on breaking down the food to its recipe and individual ingredient level. Although this approach provides a more precise estimate, it is complicated to implement and assumptions must be made about commercial products whose recipes (ingredients and the amount of each ingredient) are not readily available, thus threatening the validity of the estimated whole grain content of a food product.

To evaluate the validity of the more complex approach just described, researchers at the University of Minnesota Nutrition Coordinating Center (NCC) identified products from the bread, cracker, ready-to-eat cereal, and snack chip aisles of chain supermarkets that had grams of whole grains per serving specified on product packaging (n = 54) (14). These values served as a criterion measure of whole grain composition. Using the ingredient statement and nutrition facts panel information on the product packaging, an NCC database scientist unaware of the grams of whole grain information developed a recipe for each product. Recipes were developed using a food calculation software application routinely used at NCC to create formulations for commercial food products. The software, using a linear optimization algorithm, estimates the amount of each ingredient needed to produce a product with a nutrient profile close to that indicated on the nutrition facts panel. Because the ingredient statement lists ingredients in descending order of content in the product, the linear optimization algorithm in the software places this constraint on solutions derived for ingredient amounts. After the recipes were completed, the grams of whole grains in each product were estimated and compared with the labeled whole grain content (criterion measure). Results of this comparison indicated that the estimated values were close to the labeled values (± 4 g) for most of the products examined (45 of 52). Furthermore, the correlation between labeled and estimated values was very high (r = 0.95) (14). These results suggest it may be possible to estimate whole grain content of commercial food products with reasonable accuracy; however, the accuracy of this method needs to be tested with more complex foods.

Thus, ongoing efforts are necessary to more accurately estimate whole grain intake to gain a better representation of population and individual intakes and to more accurately substantiate their association with health and chronic disease risk reduction.

Whole grain phytonutrients

Whole grains are rich sources of vitamins, minerals, dietary fiber, lignans, β-glucan, inulin, numerous phytochemicals, phytosterols, phytin, and sphingolipids (3,15). The bran is the multi-layered outer skin of the grain that protects the germ and the endosperm from damage, such as sunlight, pests, water, and disease. The bran contains phenolic compounds, vitamins, minerals, and fiber. The endosperm is the largest component of the whole grain; it contains carbohydrates (starch), protein, vitamins, and minerals and serves as the food supply for the germ and provides energy for the rest of the plant. The germ refers to the embryo, the part that forms the new plant, and contains vitamins, some protein, minerals, and fat.

Dietary phytochemicals are defined as bioactive, non-nutrient plant compounds that are associated with reduced risk of chronic diseases (15). Adom et al. (16) reported that the majority of the beneficial phytochemicals are present in the bran and germ fractions of whole grains. Prospective cohort studies consistently suggest that when consumed in whole foods, these phytochemicals may contribute to important protection against chronic diseases, such as CVD and certain cancers (3). The additive and synergistic effects of these bioactive phytochemicals found in whole grains may be responsible for the health benefits associated with whole grains; additionally, the whole grain phytochemicals complement those in fruits and vegetables when consumed together (3,15,16).

Plant phenolic acids provide chemical defense to the plant against pathogens, parasites, and predators (15). There are various classes of phenolic compounds in whole grains, including derivatives of benzoic and cinnamic acids, namely ferulic acid, vanillic acid, caffeic acid, syringic acid, p-coumaric acid, anthocyanidins, quinines, flavonols, chalones, flavones, flavanones, and amino phenolic compounds (3,16). These phenolic acids are present in soluble-conjugated (bound) and free form in the whole grains (17). Ferulic acid is one of the most studied whole grain phenolic acids (3,16–19). Ferulic acid is most abundant in the aleurone, pericarp, and embryo cell walls of the whole grains and occurs only in trace amounts in the endosperm. Ferulic acid can exist in the free, soluble-conjugated, and insoluble bound forms in whole grains, with the bound form being the most predominant form (93% of total), than free and soluble-conjugated forms, in corn, wheat, oats, and rice (16–19). Food processing, such as thermal processing and milling, can help release these phytochemicals, making them more bioaccessible. Additionally, colonic digestion results in release of the bound phenolic compounds, thus enabling them to exert their health effects both locally and systemically upon absorption. Andreasen et al. (20) showed that human gastrointestinal esterase, from the intestinal mucosa and intestinal microbiota, can release ferulic acid and diferulics from cereal bran, thereby potentially contributing to the lower risk of certain cancers, such as colon cancer, that have been associated with whole grain consumption (21).

In wheat kernels, ferulic acid and other phenolic acids provide protection by generating physical and chemical barriers

through cross-linking with carbohydrates, antioxidant activities to combat destructive radicals, and astringency that deters consumption by insects and animals (3,16,17). The whole grain phenolic compounds in the body function as antioxidants by donating hydrogen atoms to free radicals (3,17). The total phenolic acid concentration of whole grains corresponds to their total antioxidant capacities. Corn has the highest phenolic acid content, followed by wheat, oats, and rice, with 265, 136, 111, and 95 mg gallic acid equivalents/100 g, respectively (17). Miller et al. (22) reported the antioxidant capacity of whole grain breakfast cereals to range from 2200 to 3500 Trolox equivalents (TE). In comparison, antioxidant capacity of fruits generally ranged from 600 to 1700 TE, with a high of 2200 TE for red plums and 3600 TE for berries, and vegetables averaged 450 TE, with a high of 1400 TE for red cabbage. A 41-g average serving of ready-to-eat whole grain breakfast cereal had an antioxidant capacity of 1120 TE compared with 380 and 1020 TE in an average 85-g serving of vegetables and fruits, respectively.

Carotenoids are another group of compounds found in whole grains (3,16). Lutein, zeaxanthin, β-cryptoxanthin, β-carotene, and α-carotene are the most common carotenoids and are commonly concentrated in the bran or germ portion of whole grains (3,16). In addition to providing pigmentation, they play an important role in reproduction and protection of the whole grains, while also acting as antioxidants and having provitamin A activity (β-crytoxanthin, β-carotene, and α-carotene) in the body.

Whole grains also contain tocotrienols, tocopherols, and oryzanols (3). Vitamin E, as tocopherols and tocotrienols, is found in whole grains in varying proportions and is concentrated in the germ fraction of the grain (3). β-Tocotrienol is the predominant form of vitamin E in whole wheat grain (3). An important function of vitamin E in the body is its antioxidant activity and maintenance of cellular membrane integrity. Whole grains also contain unsaturated fatty acids, mainly oleic and linoleic acid, both of which have been suggested to lower blood cholesterol levels.

Whole grains also contain fiber, RS, oligosaccharides, and lignans, which have important biological activities and functions (3,23). For example, the dietary fiber, RS, and oligosaccharides in whole grains may contribute to cholesterol reduction, healthy blood glucose and insulin concentrations, improved digestive health, and lower risk of certain gastrointestinal cancers (23). Lignans found in whole grains have strong antioxidant and phytoestrogenic effects. Intestinal microflora play a role in converting these plant lignans into the mammalian lignans, enterolactone and enterodiol, which may provide protection against chronic diseases such as hormone-related cancers, diabetes, and heart disease (3,23).

Plant sterols and stanols are also found in whole grains, the type and amount varying by the type of whole grain and the whole grain component. They are known to inhibit cholesterol absorption and increase its excretion, thereby playing a role in regulating blood cholesterol levels. Increased whole grain consumption may be associated with increased phytosterol intake, thus potentially contributing to cholesterol reduction and cardioprotection (3).

Antinutrients such as phytic acid, tannins, and enzyme inhibitors are also present in whole grains and may contribute to their overall protective effects (3,23). Phytic acid forms chelates with various metals suppressing iron-catalyzed redox reactions and associated oxidative damage. Likewise, phytic acid can suppress the oxidant damage associated with the oxygen radicals produced by the colonic bacteria, thereby protecting the intestinal epithelium. Protease inhibitors, phytic acid, phenolic acids, and saponins present in whole grain have also been suggested to lower the risk of certain cancers, such as colon cancer and breast cancer. Phytic acid, lectins, phenolic acids, amylase inhibitors, and saponins have also been shown to lower plasma glucose, insulin, and/or plasma cholesterol and TG levels (23).

In summary, whole grains have higher phytonutrient content and antioxidant activity than refined grains. Refined wheat flour loses 83% of total phenolic acids, 79% of total flavonoids, 93% of ferulic acid, 78% of total zeaxanthin, 51% of total lutein, and 42% of total β-cryptoxanthin compared with whole wheat flour (16). Further research on the health benefits of whole grain phytochemicals, their bioavailability, effects of processing on their physiological effects, and amounts in whole grain products is warranted.

Whole grains and weight management

Cross-sectional and prospective epidemiological studies indicate that consuming whole grains is associated with reduced risk of obesity and weight gain (24). To date, 14 cross-sectional studies, the majority of which were conducted in the US, have found that higher intake of whole grains (a daily intake of ~3 servings) is associated with lower BMI (kg/m^2) in adults; 3 studies observed that adults who consumed higher intakes of whole grains had smaller waist circumferences (25–38) (Table 3). McKeown et al. (25) in the Framingham Offspring Study and Newby et al. (31) in the Baltimore Longitudinal Study of Aging observed an inverse association between whole grain consumption and BMI, waist:hip ratio, and waist circumference. Generally, an ~1-unit difference in BMI is observed between the highest and lowest whole grain intakes. More recently, McKeown et al. (35) also showed that higher intakes of whole grain foods were associated, in a dose-dependent manner, with lower abdominal fat (43.0 vs. 39.4%; P-trend = 0.02), as measured by dual-energy X-ray absorptiometry, among older adults. In this study, whole grain intake in the top quintile was 3 servings/d compared with <0.5 servings/d in the lowest quintile. In contrast, no significant relationship was observed with refined-grain intake. Likewise, McKeown et al. (38) showed that whole grain consumption was inversely associated with subcutaneous and visceral adipose tissue volume among the Framingham Offspring cohort; visceral adipose tissue volume was 10.7% lower among individuals consuming 3 or more ounce-equivalent servings of whole grains per day compared with no whole grain consumption.

Prospective studies suggest that weight gain and increases in abdominal adiposity over time are lower in people who consume more whole grains. Analyses of the Physicians' Health Study (27) and the Nurses' Health Study (26) showed that those who consumed more whole grain foods consistently weighed less than those who consumed fewer whole grain foods at each follow-up period of the study. Koh-Banerjee et al. (27) estimated that for every 40-g increase in daily whole grain intake, the 8-y weight gain was lower by 1.1 kg.

In a recent cross-sectional study of adults in the UK, Thane et al. (37), using 7-d food records and defining whole grain intake as foods containing >10% whole grains, observed that higher intake was inversely associated with the percentage of men classified as obese based on BMI, independent of other factors, and intake was not associated with body weight or prevalence of overweight. Harland and Garton (24), in a systematic review of the evidence, showed modest reduction in BMI (0.63 kg/m^2) and waist circumference (2.7 cm) with the consumption of 3 servings/d of whole grains. A mean difference in BMI of ~0.5 kg/m^2 at the population level translates into a 5%

increase in the rate of coronary events. The consistency of the observational studies lends credence to an important relationship observed between whole grain intake and body weight management.

Intervention studies on the effects of whole grains on body weight and obesity-related metabolic risk factors have yielded inconsistent results, potentially because of the use of hypocaloric diet programs as part of the intervention. Katcher et al. (39) observed similar weight loss with a whole grain hypocaloric diet compared with a refined grain hypocaloric diet, but observed a greater decrease in percent abdominal body fat in the whole grain group compared with the refined grain group (−2.2 vs. −0.9%, respectively; $P = 0.03$). Interestingly, Kallio et al. (40) showed a 21% decrease in adipocyte size, in the absence of body weight changes, after the consumption of a rye pasta diet for 12 wk. However, more recently, Brownlee et al. (41), in a 16-wk dietary intervention study in healthy, overweight individuals consuming a weight maintenance diet, did not observe any changes in body weight or measures of body composition with a whole grain dietary intervention [3 servings/d (60 g/d) and 6 servings/d (120 g/d)]. The authors attributed their null findings to the nature of the intervention, the addition vs. substitution of whole grain foods into the diets, increased energy intake, and participant characteristics, among other factors (42). These intervention studies, combined with the observational studies, suggest that inclusion of whole grain foods into the diet may alter body fat distributions independently of changes in overall body weight; however, their mechanism of action still needs to be elucidated.

Several mechanisms have been suggested to explain why whole grain intake may play a role in body weight management. Fiber content of whole grain foods may influence food volume and energy density, gastric emptying, and glycemic response. Whole grains has also been proposed to play an important role in promoting satiety; individuals who eat more whole grain foods may eat less because they feel satisfied with less food. Some studies comparing feelings of fullness or actual food intake after ingestion of certain whole grains, such as barley, oats, buckwheat, or quinoa, compared with refined grain controls indicated a trend toward increased satiety with whole grains (43–45). These data are in accordance with analyses determining the satiety index of a large number of foods, which showed that the satiety index of traditional white bread was lower than that of whole grain breads (45). However, in general, these satiety studies have not observed a reduction in energy intake; hence, further research is needed to better understand the satiety effects of whole grains and their impact on weight management.

Whole grains, in some studies, have also been observed to lower the glycemic and insulin responses, affect hunger hormones, and reduce subsequent food intake in adults (46–48). Ingestion of specific whole grains has been shown to influence hormones that affect appetite and fullness, such as ghrelin, peptide YY, glucose-dependent insulinotropic polypeptide, glucagon-like peptide 1, and cholecystokinin (46–48). Whole grain foods with fiber, such as wheat bran or functional doses of high molecular weight β-glucans, compared with lower fiber or refined counterparts have been observed to alter gastric emptying rates. Although it is likely that whole grains and dietary fiber may have similar effects on satiety, fullness, and energy intake, further research is needed to elucidate how, and to what degree, short-term satiety influences body weight in all age groups.

Differences in particle size of whole grain foods may have an effect on satiety, glycemic response, and other metabolic and biochemical (leptin, insulin, etc.) responses. Additionally, whole grains have been suggested to have prebiotic effects. For example, the presence of oligosaccharides, RS, and other fermentable carbohydrates may increase the number of fecal bifidobacteria and lactobacilli (49), thus potentially increasing the SCFA production and thereby potentially altering the metabolic and physiological responses that affect body weight regulation.

In summary, the current evidence among a predominantly Caucasian population suggests that consuming 3 or more servings of whole grains per day is associated with lower BMI, lower abdominal adiposity, and trends toward lower weight gain over time. However, intervention studies have been inconsistent regarding weight loss. As recommendations are made to incorporate whole grain foods into the diet, it will be important to emphasize replacing refined grain foods with nutrient-dense, whole grain foods rather than adding more food; this will ensure that energy balance is maintained. Further research is needed to examine the relationship between whole grain intake and abdominal adiposity or weight gain in ethnic minority groups, children, and adolescents. Additionally, there is a need for longer term dietary intervention and metabolic studies in both healthy and obese adults to better understand the mechanisms of action and relationships among whole grain intake, regulation of body weight, and adiposity.

Whole grains and CVD

Epidemiological studies from North American and European cohorts have consistently shown that consumption of whole grains is associated with reduced risk of CVD (50) (Table 4). Jacobs et al. (60) observed an inverse association between whole grain intake and risk of death from ischemic heart disease in the Iowa Women's Health Study, even after adjustment for potentially confounding factors and adjustment for total dietary fiber intake (RR = 0.70; 95% CI = 0.50–0.98 for highest quintile of whole grain intake). Liu et al. (61) in the Nurses' Health Study also observed a strong inverse association between whole grain intake and risk of coronary heart disease (CHD) (RR = 0.51; 95% CI = 0.41–0.64) for women in the highest quintile of whole grain consumption compared with those in the lowest quintile. Steffen et al. (58) in the Atherosclerosis Risk in Communities study observed that 3 servings of whole grain foods per day was associated with a 28% lower risk of coronary artery disease, whereas Nettleton et al. (63) observed a 7% lower risk of incident heart failure in the same cohort. In a meta-analysis by Anderson et al. (64), which included 12 studies, data showed there was a significant inverse association between whole grain consumption and reduced risk of CHD (RR = 0.74; 95% CI = 0.64–0.84) after adjustment for primary and secondary risk factors. Additionally, the impact of whole grains on CHD risk reduction was stronger than the impact of cereal fiber alone; it was also stronger than the effect of total dietary fiber or that from fruits and vegetables. A more recent meta-analysis of 7 prospective cohort studies by Mellen et al. (65) estimated a 21% lower risk of CVD events with greater whole grain intake (2.5 servings/d vs. 0.2 servings/d); additionally, the authors recommended that, "In light of this consistent evidence, policy makers, scientist and clinicians should redouble efforts to incorporate clear messages on the beneficial effects of whole grains into public health and clinical practice endeavors."

A number of mechanisms have been suggested for the CHD risk reduction associated with whole grains. These mechanisms include: the soluble fiber component that is associated with increased fecal excretion of cholesterol and bile acid; the antioxidant and antiinflammatory properties, possibly due to

the presence of polyphenolics and other phytonutrients in whole grains; the fermentation of whole grain polysaccharides in the large bowel resulting in SCFA production, in particular propionate, which can inhibit cholesterol synthesis; and the increased serum enterolactone concentrations from fermentation of plant lignans by the gut microflora (3,23,50). Other potential mechanisms include modulating blood glucose and insulin responses, improving vascular function and blood pressure, and weight control. Cochrane Review investigated the effects of whole grains on CHD risk in participants with preexisting CHD or 1 preexisting risk factor; they concluded that there is weak evidence for the LDL-cholesterol reduction potential of whole grains (66). However, it is unclear if LDL-cholesterol lowering is the sole mechanism of action for whole grains with regards to CHD risk reduction. It is also important to note that this review focused on studies where oats were the grain used in the intervention studies. Given the variation in the active cholesterol-lowering components (i.e. soluble fiber, β-glucan, and phytonutrients such as phytosterols) of different grains, the conclusions of Kelly et al. (66) need to be interpreted cautiously.

Higher whole grain intake has been associated with reduced risk of hypertension in prospective epidemiological and intervention studies. Wang et al. (54) in the Health Professionals' Study observed a 23% less likelihood of having hypertension among men who reported consuming at least 4 daily servings of whole grain foods compared with those who consumed less than one-half serving per day. In a recent intervention study, Tighe et al. (67) reported 6- and 3-mm Hg reductions in systolic blood pressure and pulse pressure, respectively, among middle-aged healthy individuals consuming 3 servings of whole grain foods per day compared with individuals consuming refined grains. This observed decrease in systolic blood pressure is estimated to lower the risk of coronary artery disease and stroke by ≥15 and ≥25%, respectively (67). In addition to fiber, whole grains contribute nutrients such as protein, magnesium, and potassium, which have been shown to play a role in blood pressure reduction. Additionally, the antiinflammatory effects of whole grains may also contribute to lower blood pressure and CVD risk (23,42,50,65).

Mellen et al. (68) and Erkkila et al. (69) both observed a positive association between whole grain intake and improvements in coronary artery intima thickness and diameter, a measure of progression of coronary artery atherosclerosis, after adjustments for CVD, blood pressure, and other confounding factors. These studies suggest that high whole grain intake is associated with less atherosclerotic progression among individuals of multiple ethnicities and with varying cardiovascular risk profiles; this could be attributed to the plethora of beneficial components present in whole grains. These observations need to be confirmed in other studies and, if possible, the bioactive components responsible for these effects should be identified.

The role of whole grains in lowering blood lipids and lipoproteins is less clear, and the results from randomized intervention studies are variable. The evidence regarding the efficacy of oat and barley β-glucan in lowering blood lipids is well substantiated. On the other hand, the effect of whole grain foods prepared from other cereal grains in lowering blood lipids is less consistent. Brownlee et al. (41) reported the results of a randomized controlled intervention trial, which showed that whole grain foods (60 and 120 g/d) had no impact on plasma LDL-cholesterol levels of overweight but otherwise healthy adults. Furthermore, Brownlee et al. (41) observed no changes in insulin sensitivity, endothelial function, inflammatory markers, or anthropometric measures with the whole grain intervention. In contrast, Giacco et al. (70) reported a significant reduction (5%) in fasting and postprandial plasma LDL-cholesterol with the consumption of wholemeal wheat foods. Similarly, the CHEWit Study (71) and the GrainMark Study (72) both showed significant reductions in systolic blood pressure and LDL-cholesterol with higher whole grain intake. Haldar et al. (72) also reported that rye-based whole grain foods (48 g/d for 4 wk followed by 96 g/d for another 4 wk) were more effective in lowering blood cholesterol levels compared with wheat-based foods, which may be attributed to the higher soluble fiber content of rye compared with wheat. Discrepancies in these studies could be due to the fact that whole grain foods were potentially added to the diet rather than substituted for refined grain foods, as intended in the Brownlee study, because an increase in energy intake was observed in the intervention group compared with the control group and participants, although overweight, did not have elevated blood lipid concentrations at the start of the study. Overall, these intervention studies raise several important issues, namely, conducting randomized controlled intervention studies is challenging and changing diets in free-living intervention studies is not easy, particularly with complex food-based systems, wherein the benefits and interactions of the different components are still not well understood. Compliance with dietary interventions will always be an issue and biomarkers of intake are critical to enable better quantification of intake. Importantly, the study by Brownlee et al. (41) raises the question about the use of volunteers who are at risk compared with healthy individuals in regards to the study objectives and expected outcomes.

C-reactive protein (CRP), an acute-phase protein that is a sensitive marker of subclinical inflammation, has been shown to be strongly associated with risk of CVD, type 2 diabetes, and cancer (73,74). Whole grain intake has been associated with lower concentrations of CRP in epidemiological and intervention studies. Qi et al. (75) in the Nurses' Health Study observed that whole grain intake was associated with improved inflammatory status among women with type 2 diabetes and the highest whole grain intake was associated with lower CRP and TNFα levels compared with the lowest whole grain intake. Similar observations were made in the Insulin Resistance Atherosclerosis Study (76). The Multi-Ethnic Study of Atherosclerosis (30) and the Nurses' Health Study (51) reported significant inverse associations between whole grain intake and CRP concentrations even after adjustment for several confounding factors; similar associations were more recently observed among younger women (77). In a controlled weight loss intervention study, Katcher et al. (39) observed a 38% reduction in CRP concentrations among obese individuals consuming a whole grain hypocaloric diet compared with a refined grain hypocaloric diet. These effects of whole grains have been attributed to the synergistic, antiinflammatory effects of the dietary fiber, minerals, antioxidants, polyphenols, and other phytonutrients present in whole grain.

Preliminary studies also suggest that whole grain intake may be associated with improvements in insulin sensitivity (30,78), a risk factor associated with CHD. It was reported that habitual consumers of primarily whole grain flour products had lower fasting insulin concentrations than habitual refined grain flour consumers. Pereira et al. (78) observed that fasting insulin was 10% lower during consumption of the whole grain diet than during consumption of the refined grain diet (mean difference: -15 ± 5.5 pmol/L; $P = 0.03$) and the area under the 2-h insulin curve tended to be lower than after the refined grain diet. The higher fiber and indigestible carbohydrate content in many

whole grain foods may be fermented by colonic bacteria, which may produce SCFA that enter the portal circulation and influence hepatic glucose oxidation, decrease fatty acid release, and increase insulin clearance, thereby improving insulin sensitivity. Pereira et al. (78) also suggested that a high-whole grain, high-fiber diet could improve insulin receptor sensitivity through a chronic lowering of the overall dietary glycemic index and related insulin secretion as well as through SCFA production, leading to enhanced hepatic glucose oxidation and insulin clearance.

Based on the existing evidence, there are 4 consensus authoritative statements from national organizations, namely the U.S. FDA (79), the U.K. Joint Health Claims Initiative (80), and the Sweden (81) and Danish Dietary Recommendations (82) that link consumption of whole grains with improved heart health. Dietary guidelines around the world emphasize the importance of grain foods, particularly whole grains in the diet. For example, U.K. products composed of ≥51% whole grains can claim, "People with a healthy heart tend to eat more whole grains foods as part of a healthy lifestyle." In Sweden, products with at least 50% whole grains can state, "A healthy lifestyle and a balanced diet rich in whole grains products reduce the risk of heart disease. Product X is rich in whole grains."

In summary, the current scientific evidence is strong and consistent to suggest that whole grains have a beneficial effect on CVD risk reduction. Further research is needed to better understand the mechanism of action and the impact of the various components of whole grains on CVD risk reduction.

Whole grains and type 2 diabetes

Type 2 diabetes is an epidemic that affects an ever-increasing proportion of the U.S. and global population. The interactions among genes, environment, diet, and lifestyle all play an important role in insulin resistance and the subsequent multifactorial pathogenesis of diabetes. Lifestyle modification and weight control are major factors in the prevention and treatment of diabetes. Gross et al. (83) suggested that increased intake of refined carbohydrates, along with decreased intake of fiber, contributes to the increasing prevalence of type 2 diabetes in the US.

Evidence from epidemiological studies shows an inverse association between whole grain consumption and risk of type 2 diabetes. In a prospective cohort study, Liu et al. (84) found that increased intake of whole grains significantly lowered the risk of type 2 diabetes, after adjusting for age and energy intake, when comparing the highest quintile of whole grain intake to the lowest quintile (RR = 0.62; 95% CI = 0.53–0.71). An examination of dietary patterns revealed that a prudent diet, characterized by high consumption of whole grains, legumes, fruits, vegetables, seafood, white meat, nuts, and vegetable oils, was inversely associated with risk of type 2 diabetes, whereas a Western diet, characterized by high consumption of refined grains, red meat, processed meat, potatoes, and food high in saturated fat, cholesterol, and *trans* fat, was positively associated with risk of type 2 diabetes (85). A recent meta-analysis by de Munter et al. (86) showed that a 2-serving/d increase in whole grain consumption is associated with a 21% (95% CI = 13–28%) decrease in risk of type 2 diabetes after adjustment for potential confounders and BMI.

Gross et al. (83) suggested that the beneficial effects may be due to the structure of whole grains and the nutrients found in whole grains such as dietary magnesium and antioxidants like vitamin E, phytic acid, and selenium. Whole grain particle size influences rate of digestion and consequent metabolic effects and thus affects the etiology and management of diabetes. An in vitro study by Heaton et al. (87) showed step-wise increases in insulin responses based on the nature of the whole grains: whole grains < cracked grains < coarse flour < fine flour. Among overweight and obese individuals, Pereira et al. (78) observed 10% lower fasting insulin and 13% lower measures of insulin resistance after 6 wk of consumption of a whole grain diet compared with a refined grain diet, thus suggesting improved insulin sensitivity.

In summary, dietary patterns characterized by refined carbohydrates may adversely affect metabolic intermediates and such a diet may increase the risk of vascular diseases, such as diabetes and CHD, especially among individuals prone to insulin resistance. To lower disease risk and improve vascular health outcomes, it is imperative to replace refined grains with whole grains to improve glucose homeostasis. Future research needs to examine the interactions not only among different dietary factors but also between diet and genetic predisposition and between diet and metabolic determinants, such as physical activity. It will be important to conduct randomized intervention trials of sufficient size and length to further elucidate the role of whole grains and associated components in diabetes risk reduction.

Whole grains and gastrointestinal health

Gastrointestinal health is characterized as maintenance of homoeostasis of gastrointestinal function by promoting efficient digestion, optimal gut immune responses, minimal inflammation, and the absence of disease. However, given the continuous and regular exposure of the gastrointestinal tract to pathogens and toxins from the external environment, it is challenging to maintain homeostasis and gastrointestinal health. Prevalence data show that gastrointestinal diseases have significantly risen (>30%) between 1992 and 2004, contributing to $142 billion in total medical costs (88). Colorectal cancer is the 4th most common type of cancer, contributing to 53% of all gastrointestinal cancers (89). Current prevalence data suggest that there are many factors affecting gastrointestinal health, including, lifestyle, diet, environment, genetics, and age.

Epidemiological studies have shown an inverse association between whole grain consumption and relative risk of certain cancers (21). Observational studies in the US and Europe suggest a strong inverse association between whole grain consumption and gastrointestinal cancers, certain hormone-related cancers and pancreatic cancer. In prospective studies, Larsson et al. (90), in the Swedish Mammography cohort, reported a 24% lower risk of colorectal cancer in the highest quintile of whole grain intake compared with the lowest quintile, and Schatzkin et al. (91), in the NIH-AARP Diet and Health Study cohort, observed a 21% reduction in risk of colorectal cancer in the highest quintile of whole grain intake compared with the lowest quintile. In a recent meta-analysis, Haas et al. (92) observed an inverse relationship between consumption of whole grains and risk of developing colorectal cancer; further work is needed to better understand this association.

Many dietary components can positively affect gastrointestinal health, including fiber, RS, oligosaccharides, phytochemicals, antioxidant vitamins, and minerals. Of the myriad of foods available, whole grains provide most of these beneficial components. Whole grains play an important role in digestive health and this is attributed to not only the fiber component but also the other nutrients and phytonutrients present in the whole grains. Whole grains contain a significantly higher proportion of nutrients than their refined grain counterparts (3). The dietary fiber components of whole grains vary from one grain to another (Table 2) (93), with the whole grain version having higher

proportions than the refined grain version. Additionally, different grains have different proportions of soluble and insoluble fibers, with whole grain wheat being lower in soluble fiber compared with whole grain oats, rye, and barley.

The fiber components of whole grains include fermentable carbohydrates, namely soluble and insoluble dietary fiber, RS, and oligosaccharides. Two types of oligosaccharides exist in cereal grains, galactosyl derivates of sucrose (stachyose and raffinose) and fructosyl derivates of sucrose (fructooligosaccharides) (94), which are present in the bran and germ components of the whole grain. Some dietary fibers play a role in maintaining gastrointestinal health by increasing fecal bulk, increasing transit time, increasing removal of carcinogenic compounds, increasing binding to mutagens, increasing SCFA production, and lowering colonic pH (95). Coarse wheat bran has a greater fecal bulking effect than finely ground wheat bran when fed at the same dosage (96), suggesting that particle size of the whole grain is an important factor in determining its physiological effect. McIntyer et al. (97) suggested that the coarse nature of whole grain compared with refined grain results in a unique physiological effect beyond compositional differences between whole and refined grains.

There is considerable evidence regarding the fermentable carbohydrates in whole grains and their role in gastrointestinal function and health. Disruption of cell walls increases fermentability of the dietary fiber in the whole grains and the release of phytonutrients, which, in combination, can aid in digestive health. Undigested carbohydrate that reaches the colon may be fermented by intestinal microbiota to SCFA, including acetate, propionate, and butyrate. These SCFA, namely butyrate, serve as energy sources for the colonic mucosal cells and the gut microbiota, while also influencing other systemic metabolic and physiological processes such as the role of propionate in hepatic lipid metabolism.

Whole grains are also a concentrated source of RS. There are 4 main types of RS: RS1, which is the physically inaccessible starch present in whole or partly milled grain; RS2, which is the large resistant granule present in high amylose-containing grains, raw potatoes, and green bananas; RS3, which is the retrograded starch present in cooked and cooled grain and breads; and RS4, which is the chemically modified form present inesterified or cross-bonded starch. The RS content of raw whole grains varies; e.g., in vitro studies in canine models indicate that corn contains 31%, wheat 27%, and barley 33% (93), with the respective flours having considerably lower amounts. RS has been proposed to play a role in gastrointestinal health by increasing fecal bulk by ~1–1.7 g additional feces/g of RS consumed, increasing microbial mass, and increasing prebiotic effects, thereby increasing beneficial bacteria and decreasing pathogens, increasing SCFA production, especially butyrate, and decreasing production of toxic metabolites such as ammonia and deoxycholic acid (98).

The SCFA butyrate is the primary metabolic fuel for the colonic epithelial cells and is essential for maintaining epithelial health. Butyrate may contribute to gastrointestinal health by lowering inflammation, oxidative stress, and diarrhea and increasing barrier function, mineral absorption, and detoxifying enzyme activities (98). Hernot et al. (99) showed that butyrate production is proportional to the RS content of whole grains, with wheat and corn being the highest producers, followed by barley and oats, and rice being the lowest butyrate producer. It has been suggested that the insoluble fiber content of whole grains may aid in the fermentation of RS in the distal colon, thus allowing for a more uniform production of butyrate and a potential protective mechanism against tumor development and growth.

A prebiotic is defined as "a selectively fermented ingredient that allows specific changes, both in the composition and/or activity in the gastrointestinal microbiota that confers benefits upon host well-being and health" (100). Whole grains have been suggested to have prebiotic effects. The oligosaccharides and the RS present in whole grains qualify for this prebiotic status. These prebiotics selectively increase beneficial bacteria in the gut, mainly bifidobacteria and lactobacilli. By altering this beneficial gut microbiota, the fermentable carbohydrates can influence host immune response, specifically by influencing the gut-associated lymphoid tissue. In vitro studies by Karppinen et al. (101) showed that inulin, a fructose polymer, was fermented faster than the more complex carbohydrates in cereal bran. Oat bran, rich in β-glucan, was fermented faster than rye and wheat brans, which are rich in arabinoxylans. Costabile et al. (49) conducted a double-blind, randomized crossover study of whole grain wheat and wheat bran in 31 human participants. After 3 wk of each dietary intervention, fecal bifidobacteria and lactobacilli were significantly higher with whole grain wheat consumption compared with wheat bran consumption; this prebiotic activity may contribute to the beneficial physiological effects of whole grain wheat. However, there were no significant differences in fecal SCFA production with ingestion of either whole grain or wheat bran. Hernot et al. (99) examined the fermentation profiles of native whole grains (barley, corn, oat, rice, and wheat) and their processed and bran components. Processing of most substrates resulted in higher dry matter and starch digestibility and lower RS concentrations. Dietary fiber composition varied among substrates with processing. Digestion profiles for most of the whole grains and their processed and bran components correlated well with their chemical composition. Corn bran and rice substrates were the least fermentable; extrusion rendered barley, corn, and wheat more hydrolytically digestible, and barley and oat more fermentatively digestible, which can thus affect their physiological functions such as cholesterol reduction vs. intestinal barrier protection. Except for corn bran, all components had greater or equal fermentability compared with their native whole grain.

Micronutrients such as folate and vitamin B-6, polyphenols, and antioxidant compounds, along with prebiotics such as inulin, oligosaccharides and immune modulators such as β-glucan, present in whole grains potentially work synergistically to lower oxidative stress, inflammation, and pathogen load. Thus, it is the sum of the parts of whole grains that likely maintain gastrointestinal health.

In summary, whole grains provide the gastrointestinal tract with more than fiber, thus contributing to their role in maintaining gastrointestinal function and protection against disease. The various components present in whole grains may act synergistically to help improve bowel function and provide protection against gastrointestinal cancers, inflammation, and other disease states while strengthening barrier function and providing immune support. Increasing intake of whole grains is highly recommended for improving gastrointestinal health. Future research is needed to better understand the mechanism of action of whole grains in gastrointestinal health.

Summary and Conclusions

Existing evidence indicates that whole grains have a beneficial health effect; much of the evidence comes from observational studies that have demonstrated an association between

whole grain intake and disease risk reduction. Evidence from intervention studies is variable. There is consistent epidemiological evidence that whole grain foods substantially lower the risk of chronic diseases such as CHD, diabetes, and cancer and also play a role in body weight management and digestive health. The essential macro- and micronutrients along with the phytonutrients present in whole grains synergistically contribute to their beneficial effects. Current evidence lends credence to the recommendations to incorporate whole grain foods into a healthy diet and lifestyle program. Future research needs to examine the role of whole grain foods in disease prevention and management to gain a better understanding of their mechanisms of action. Given the current evidence, the importance of whole grains in the diet of individuals is best summarized by Dr. Chris Seal, who very elegantly states, "When shopping in a supermarket there will be a range of healthy, nutritious whole grains foods, be sure to get them and beware of spurious imitations. After a little time their taste grows on you and refined foods will no longer satisfy you. Soon, only the ill-informed will avoid whole grains foods. Whole grains are not a luxury, and no house is complete unless they are provided at every meal (Dr. Chris Seal, Newcastle University, personal communication)."

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