The Role of Whole Grains in Body Weight Regulation\textsuperscript{1,2}

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ABSTRACT

Whole grain (WG)-rich diets are purported to have a variety of health benefits, including a favorable role in body weight regulation. Current dietary recommendations advocate substituting WG for refined grains (RG), because many of the beneficial bioactive components intrinsic to WG are lost during the refining process. Epidemiological studies consistently demonstrate that higher intakes of WG, but not RG, are associated with lower BMI and/or reduced risk of obesity. However, recent clinical trials have failed to support a role for WG in promoting weight loss or maintenance. Though the biochemical and structural characteristics of WG have been shown to modulate appetite, nutrient availability, and energy utilization, the capacity of WG foods to elicit these effects varies with the type and amount of grain consumed as well as the nature of its consumption. As such, WG foods differentially affect physiologic factors influencing body weight with the common practice of processing and reconstituting WG ingredients during food production likely mitigating the capacity for WG to benefit body weight regulation. Adv. Nutr. 3: 697–707, 2012.

Introduction

Obesity is a predominant public health concern\textsuperscript{(1,2)} with related health care costs now estimated at more than $190 billion annually in the United States\textsuperscript{(3)}. Diet composition is among many lifestyle factors contributing to the development of obesity and associated chronic diseases, including cardiovascular disease, cancer, and type 2 diabetes. As such, identifying dietary patterns, or individual foods and nutrients that should be increased or decreased in the diet to prevent and treat obesity, is an important public health strategy. Consuming whole grains (WG)\textsuperscript{3} is postulated to decrease chronic disease risk, in part due to beneficial effects on body weight regulation\textsuperscript{(4–6)}.

The American Association of Cereal Chemists (AACC) defines a WG food ingredient as consisting of the “intact, ground, cracked or flaked caryopsis (kernel) whose principal components—the starchy endosperm, germ, and bran—are present in the same relative proportions as they exist in the intact caryopsis”\textsuperscript{(7)}. Slight derivations of this definition have been proposed and a recognized need for an internationally accepted definition exists\textsuperscript{(8)}. Caryopses are the edible seeds of cereal crops that consist of 3 primary anatomical components: endosperm, germ, and bran. The endosperm comprises the largest portion of the grain, consisting primarily of storage proteins and starches needed to feed the germ during maturation\textsuperscript{(6)}. The germ contains the embryo and the bran acts as a multi-layered protective barrier for the grain\textsuperscript{(9)}. Though fiber, vitamins, minerals, and other phytochemicals are present throughout the grain, the bran and germ are more concentrated sources than endosperm\textsuperscript{(9)}.

The most commonly consumed WG worldwide are wheat, brown and long-grain rice, maize, oats, barley, rye, millet, sorghum, and triticale\textsuperscript{(9)}. Currently, these grains are more commonly processed (e.g., milled, cracked, rolled, ground, crushed, and flaked) and reconstituted before consumption than consumed in their intact form\textsuperscript{(10)}. Refined cereal grains (RG) are not fully reconstituted after processing and consist primarily of endosperm retained after the separation and removal of the bran and germ. Although the refining process improves the texture and stability of grain-based food products, much of the nutritive value of the WG is lost. Importantly, the AACC definition of a WG ingredient requires that the endosperm, bran, and germ isolated from the WG during processing be reconstituted in the
same relative proportions as exists in the intact native grain. Thus, WG are generally richer in dietary fiber, vitamins, minerals, phytoestrogens, phenolic compounds, and phytic acid relative to their refined counterparts (11). The AACC definition, however, does not stipulate that the WG structure remain intact, nor does it limit the degree of processing or minimum particle size of the WG.

The superior nutritive value of WG relative to RG and associations of increased WG intake with reduced cardiovascular disease (12,13), cancer (14,15), and type 2 diabetes risk (16) underpin dietary recommendations worldwide encouraging WG consumption. The 2010 Dietary Guidelines for Americans (17) recommend substituting WG for RG to consume at least 1.5 ounce-equivalents WG 1000 kcal$^{-1} \cdot d^{-1}$ (≥24 g WG $\cdot$ 4185 kJ$^{-1} \cdot d^{-1}$). Similarly, a number of European countries (18–23), Australia (24), and Canada (25) have recommendations encouraging intake of WG foods. Concomitant to these recommendations, the number of WG-containing food products introduced into the U.S. marketplace, e.g., has considerably increased over the past decade (26). However, WG consumption remains well below recommended levels for many (27), especially in the United States (28,29). In this review, we examine the evidence for a role of WG in body weight regulation.

**WG and body weight regulation: observational studies**

Jonnalagadda et al. (4) recently described issues associated with estimating and comparing WG intakes in observational studies. Briefly, definitions of WG foods have varied across studies, with the most commonly used definitions being derivations of that proposed by Jacobs et al. (30). This definition includes food items such as dark bread, brown rice, oatmeal, popcorn, and breakfast cereals containing ≥25% WG or bran by weight. Added germ and bran are frequently included in the definition as well. This definition contrasts with the less commonly employed U.S. FDA definition used for health claims, which requires a WG food be ≥51% WG by weight and contain germ, bran, and endosperm in the same relative proportions as are found in the intact grain. The amount of WG in a serving of a WG food therefore varies based on the definition used in addition to the relative proportion of WG to RG in the food. The fact that the exact relative proportion of WG and RG grain ingredients is proprietary information and often unknown further complicates attempts to accurately quantify WG intake (4). Thus, WG intake may be under- or overestimated, resulting in misclassification and bias.

Despite differences in the definitions and methods used to estimate WG intake, the bulk of the epidemiological evidence suggests that WG have a beneficial role in body weight regulation. A 2008 meta-analysis of cross-sectional studies examining associations between WG intake and BMI summarized 15 studies including 119,829 primarily European and American adults (31). Harland et al. (31) documented a 0.6-kg/m$^2$ lower BMI in individuals categorized as reporting the highest (~3 servings/d) compared with the lowest (<0.5 servings/d) WG intakes. The inverse association between WG intake and BMI was consistent, documented in 12 of the 15 studies reviewed (30,32–45), and is supported by recent reports (16,29,46–50). For example, using the Baltimore Longitudinal Study of Aging cohort Newby et al. (49) documented a 0.7-kg/m$^2$ lower BMI in individuals in the highest (2.8 servings/d) relative to lowest (<1 serving/d) quintile of WG intake. Likewise, McKeown et al. (47) reported a 1.1-kg/m$^2$ lower BMI in individuals in the highest (2.9 servings/d) relative to lowest (0.1 servings/d) quintile of WG intake within a subset of the Framingham Heart Offspring and Third Generation cohorts. Nearly identical results were documented in a cohort of older adults with a 1.0-kg/m$^2$ lower BMI being observed in individuals in the highest (2.9 servings/d) relative to lowest (0.2 servings/d) quartile of WG intake (48). Of note, the inverse associations between WG intake and BMI observed in these cross-sectional studies do not appear to simply reflect a beneficial effect of total grain intake on body weight regulation, because positive (33,35,47) or null (30,36–38,48,49) associations between RG intake and BMI were reported.

Prospective cohort studies support a role for WG in attenuating weight gain (32,34,35). Liu et al. (35) used the Nurses Health Study cohort to examine relationships between changes in WG and RG intakes, weight change, and obesity risk. Following 12 y of follow-up, women in the quintile representing the largest increase in WG intake (0.9 servings $\cdot$ 4185 kJ$^{-1} \cdot d^{-1}$) compared with those in the quintile representing the largest decrease in WG intake (−0.6 servings $\cdot$ 4185 kJ$^{-1} \cdot d^{-1}$) experienced a 0.4-kg lower weight gain (4.1 vs. 4.5 kg) and 19% lower odds of developing obesity (35). In contrast, women with the largest increase in RG intake (0.9 servings $\cdot$ 4185 kJ$^{-1} \cdot d^{-1}$) experienced a 0.4-kg greater increase in body weight (4.7 vs. 4.3 kg) and 18% higher odds of developing obesity compared with those with the largest reduction in RG intake (−0.9 servings $\cdot$ 4185 kJ$^{-1} \cdot d^{-1}$) (35). Similarly, Koh-Banarjee et al. (34) used the Health Professionals Follow-up Study cohort to examine relationships between WG and RG intakes and weight gain by categorizing men into quintiles of change in WG or RG intake. After 8 y of follow-up, a 0.5-kg lower weight gain (0.7 vs. 1.2 kg) was observed in men reporting the greatest increase in WG intake (1.5 servings/d) compared with those with the largest decreases in WG intake (−0.9 serving/d) (34). No benefit of RG intake on prospective weight change was documented (34). Finally, in the Physicians’ Health Study, consumption of ≥1 serving/d compared with <1 serving/wk of WG breakfast cereals was associated with a 0.4-kg lower weight gain over 13 y (1.9 vs. 2.3 kg) in age-adjusted models (32). In this study, a 0.4-kg lower weight gain (1.8 vs. 2.3 kg) was also observed in men consuming ≥1 serving/d of RG breakfast cereals compared with those who reported consuming these cereals <1/wk (32).

In addition to beneficial effects on body weight, WG consumption may be associated with reduced abdominal adiposity. In a subset of studies included in the meta-analysis...
of Harland et al. (31), the highest WG consumers were determined to have a 2.7-cm lower waist circumference (WC) and 0.02 lower waist:hip ratio compared with the lowest WG consumers. McKeown et al. (47,48) recently advanced these findings by reporting associations between WG intake and direct measures of adiposity obtained by DXA and computed tomography. Older adults in the highest (2.9 servings/d) relative to lowest (0.2 servings/d) quartile of WG intake had 2.4% lower total body fat and 3.6% lower trunk fat (48). Within a subset of the Framingham Offspring cohort, visceral adipose tissue volume as measured by computed tomography was 10% lower in individuals in the highest (2.9 servings/d) compared with lowest (0.1 servings/d) quintiles of WG intake (47). Interestingly, no association between WG intake and visceral adiposity was observed in individuals consuming ≥4 daily servings of RG, suggesting that high RG intake may counter any benefits of WG on body weight regulation (47). Few prospective cohort studies have directly examined associations between WG intake and central adiposity. In 2 separate studies, Halkjaer et al. (51,52) reported no association between intake of WG food products (51) or breads (52) and prospective WC change in Danish adults, but they noted a positive association between intake of RG food products or breads and WC change in women.

In summary, observational studies strongly suggest that consuming ~3 servings/d WG is associated with lower BMI and central adiposity relative to low or no WG consumption, and higher WG intakes may attenuate weight gain. These relationships appear to be specific to WG, because intake of RG have not generally been associated with lower BMI or adiposity in these studies. Of note, the meta-analysis of Harland et al. (31) demonstrated that higher WG intakes were associated with both increased energy and dietary fiber intakes and lower smoking prevalence. The greater energy intakes observed in high WG consumers is likely associated with the trend for higher prevalence of exercise also reported in these individuals (31). Further, Harland et al. (31) noted trends for higher micronutrient intakes and supplement use and lower saturated fat intakes in the highest compared with lowest WG consumers. Recent reports are generally consistent with these findings, demonstrating that high WG consumers tend to be more physically active, smoke less, and consume more fruit, vegetables, and dietary fiber than low WG consumers (46,47,49,53). Further, cluster and factor analyses frequently link WG consumption with dietary patterns that include high fruit and vegetable intake and that are associated with other desirable health behaviors (54,55). Although statistical adjustment for these lifestyle factors is common, the potential for residual confounding remains; therefore, associations between high WG intake and lower BMI may be mediated by healthier lifestyles of WG consumers.

**WG and body weight regulation: clinical trials**

A number of recent randomized controlled trials investigating the effects of consuming WG relative to RG on biomarkers of health status have reported changes in appetite, energy intake, body weight, or body composition as primary or secondary outcomes following incorporation of WG into diets consumed ad libitum or into energy-restricted diets for weight loss. Ad libitum intake studies commonly incorporated ≥48 g WG/d (3 ounce-equivalents/d) or a similar amount of RG derived from a variety of sources (56–60) or single food items such as WG breakfast cereal (61–63) or bread (64) into participant diets over 2–52 wk. Only 2 of these studies reported perceived appetite or ad libitum energy intake as primary outcomes (Table 1) (63,64). Isaksson et al. (63) documented postprandial reductions in perceived appetite following consumption of a WG rye breakfast porridge providing 55 g WG/d compared with refined wheat bread. This effect persisted after daily consumption of the porridge for 3 wk but did not translate into reduced energy intake or weight loss (63). In a pilot study of 14 participants, Bodinham et al. (64) observed no differential effects on perceived appetite or ad libitum energy intake over 3 wk in which WG wheat rolls providing 48 g/d WG or RG rolls were added to habitual diets. Similarly, no evidence for a spontaneous reduction in energy intake or body weight in response to WG interventions was observed in any study in which these measures were reported as secondary outcomes (56–61,65,66). However, all but 3 of these studies (61,65,66) appear to have encouraged body weight maintenance or adherence to habitual diets (excepting the intervention component) throughout the intervention (Table 1). Therefore, the reported results cannot reliably assess whether increased WG consumption should be expected to promote a spontaneous reduction in energy intake and weight loss. Two of the trials in which no recommendations regarding energy intake were given were ≤3 wk duration and therefore too short to infer effects on body weight outcomes (61,66). Ross et al. (66) did, however, report energy intake, documenting no significant effect on energy intake while substituting 150 g/d WG for RG into a diet in which all foods were provided over 2 wk. In another study, Brownlee et al. (65) attempted to investigate the effects of substituting 60 g/d or 120 g/d of WG from a variety of sources for RG on cardiovascular risk factors to include body weight and adiposity. The authors noted that volunteers more often appeared to add rather than substitute WG into their habitual diets, with energy intake increasing concomitant with WG intake. No significant changes in body weight or body fat were documented in any group (65).

Recent studies have also examined whether incorporating WG into energy-restricted diets enhances weight loss beyond energy restriction alone (67–71). Taken together, these studies provide no evidence that a hypoenergetic diet that includes ~3–7 daily servings of WG (48–112 g/d WG) promotes greater weight loss than a low-WG hypoenergetic diet (Table 1). However, in 2 of 3 studies in which body fatness was directly measured using DXA (67,68) or hydrostatic weighing (71), hypoenergetic WG-containing diets were associated with a greater reduction in body fat, primarily from the abdominal region, relative to hypoenergetic low-WG.
Table 1. Clinical studies of WG intake and energy regulation

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design and population</th>
<th>Intervention</th>
<th>Fiber intake, g/d</th>
<th>Δ Weight, kg</th>
<th>Δ Body composition</th>
<th>Appetite/Δ energy intake, kJ/d</th>
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</thead>
<tbody>
<tr>
<td><strong>Energy intake ad libitum</strong></td>
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<tr>
<td>Bodinham et al. (64)</td>
<td>3 wk CO; n = 14 Nrmwt M/F, 26 y</td>
<td>WG: 48 g WG/d, milled wheat bread C: RG bread</td>
<td>WG: 30* Ø</td>
<td>C: 26</td>
<td>BF: Ø</td>
<td>Ø / C: +368</td>
</tr>
<tr>
<td>Brownlee et al. (65)</td>
<td>16 wk RCT; n = 266 Ovwt and Ob M/F, 18–65 y</td>
<td>WG1: 60 g WG/d for 8 wk + 120 g WG/d for 8 wk² WG2: 60 g WG/d for 16 wk² C: no intervention</td>
<td>WG1: +11* Ø</td>
<td>WG1: +0.2</td>
<td>BF:</td>
<td>Not measured</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>WG2: +0.7 C: 0</td>
<td>C: +0.3%</td>
<td>C: +0.3%</td>
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<tr>
<td>Carvalho-Wells et al. (61)</td>
<td>3 wk CO; n = 32 Nrmwt, Ovwt, and Ob M/F, 20–51 y</td>
<td>WG: 48 g WG/d, maize semolina breakfast cereal C: RG breakfast cereal</td>
<td>WG: 14** C: 3</td>
<td>Ø</td>
<td>BF: Not measured</td>
<td>Not measured</td>
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<td>Isaksson et al. (63)</td>
<td>3 wk CO; n = 24 Nrmwt M/F, 18–60 y</td>
<td>WG: 55 g WG/d, cut and rolled rye porridge C: RG wheat bread</td>
<td>WG: 21 Ø</td>
<td>C: 15</td>
<td>Not measured</td>
<td>Ø</td>
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<tr>
<td>Ross et al. (66)</td>
<td>2 wk CO; n = 17 Nrmwt M/F, 20–50 y</td>
<td>WG: 150 g WG/d² C: RG foods</td>
<td>WG: 32* C: 19</td>
<td>WG: −0.05</td>
<td>C: Not measured</td>
<td>Not measured</td>
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</tbody>
</table>

**Energy intake restricted**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design and population</th>
<th>Intervention</th>
<th>Fiber intake, g/d</th>
<th>Δ Weight, kg</th>
<th>Δ Body composition</th>
<th>Appetite/Δ energy intake, kJ/d</th>
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<tr>
<td>Katcher et al. (67)</td>
<td>12 wk RCT; n = 47 Ob M/F with MetS, 20–65 y</td>
<td>WG: 4–7 oz-eq WG foods/d² C: Avoid WG foods All: 2090 kJ/d (500 kcal/d) energy deficit + DG 2005 + activity</td>
<td>WG: 21* C: 15</td>
<td>WG: −3.7</td>
<td>BF:</td>
<td>Not measured</td>
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<tr>
<td>Kristensen et al. (68)</td>
<td>12 wk RCT; n = 72 Ovwt and Ob postmenopausal F, 45–70 y</td>
<td>WG: 105 g WG/d² C: RG foods All: 1254 kJ/d (300 kcal/d) energy deficit</td>
<td>WG: 11** C: 4</td>
<td>WG: −36</td>
<td>BF:</td>
<td>Not measured</td>
</tr>
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(Continued)
diets despite conferring no additional weight loss benefit (67,68). Katcher et al. (67) randomly assigned 50 obese adults with metabolic syndrome to receive dietary advice to obtain all recommended daily grain servings from either WG or non-WG sources while reducing energy intake 2090 kJ/d (500 kcal/d) from weight maintenance requirements. The group receiving the advice to increase WG intake averaged 5 servings/d WG compared with <0.25 servings/d in controls. Although reductions in total body fat, abdominal fat, and WC were observed in both groups after 12 wk, the abdominal fat loss was 1.3% greater in the WG group (67). In another trial, Kristensen et al. (68) instructed overweight and obese postmenopausal women to reduce energy intake by ≥1255 kJ/d (300 kcal/d) from weight maintenance requirements and to consume ~1985 kJ/d (475 kcal/d) of either WG or RG foods that were provided to participants. Total body and central fat mass and WC were reduced in both groups; however, decreases in total fat mass were significantly greater and decreases in central fat mass tended to be greater in women consuming the WG-rich diet (68). In contrast, substituting 84 g/d oats for RG wheat in a hypoenergetic diet did not differentially affect body fat loss over 6 wk in healthy adults (71). The inclusion of normal-weight participants, a greater energy deficit of 4185 kJ/d (1000 kcal/d), type of grain used, or shorter duration of this study may account for the discrepant results.

In summary, recent clinical trials provide little evidence for an effect, beneficial or detrimental, of WG intake on body weight regulation. When WG are added to or substituted for RG in ad libitum diets, no spontaneous reduction in energy intake or body weight is observed. Likewise, on the background of a hypoenergetic diet for weight loss, substituting WG for RG does not appear to promote body weight loss beyond energy restriction alone. In 2 separate studies, WG-rich hypoenergetic diets appeared to be associated with greater losses of body fat or central body fat. However, the observed effect sizes were small, within the measurement error of the methods used to assess fat mass (72–74), and not always consistent with changes in WC (67,68). These findings should therefore be considered preliminary but warrant further investigation.

Factors mediating physiological effects of WG relevant to the regulation of body weight and composition

The structural and physicochemical properties of WG are diverse and made more so when incorporated into foods. This diversity is the result of the varied chemical compositions and quantities of indigestible carbohydrates within different WG, the degree to which grains are processed prior to consumption, the methods by which WG foods are prepared, and interactions with the food matrix (75). Together, these factors mediate the physiological effects of WG and may in turn differentially influence short-term appetite regulation and nutrient utilization, thereby altering WG-mediated effects on the regulation of body weight and composition (Fig. 1).
Chewing

The fiber content, particle size, and structural integrity of WG alter the amount of chewing required for ingestion of WG foods (76,77). Increased chewing may promote satiety by enhancing gastric distention (78), augmenting gut hormone responses (79,80), prolonging orosensory stimulation (81), or slowing eating rate (82,83).

Energy density and availability

WG foods generally have a lower energy density, defined as digestible energy per unit weight, than comparable RG foods. This effect derives from the low digestible energy per unit mass (84) and water-holding capacities of dietary fibers intrinsic to many WG. Short-term studies have demonstrated that humans have a tendency to eat a consistent weight of food irrespective of energy content, indicating that from meal to meal, appetite is inconstantly determined by the mass of food than by the amount of energy consumed (85–87). Consequently, decreasing dietary energy density results in a reduction in energy intake without a concomitant increase in hunger (88,89).

The magnitude of the reduction in energy density that can be achieved using WG, however, varies with the amount and type of fiber present in the grain. WG contain both nonfermentable fibers, which provide no digestible energy, and fibers that are fermented to varying degrees by colonic microbes salvaging otherwise unavailable energy in the form of SCFA. Further, viscous fibers present in varying amounts within different WG decrease digestible energy by impairing macronutrient digestion and absorption, leading to energy excretion (90,91).

Energy digestibility has been shown to decrease by 3–4% following 20- to 25-g/d increases in dietary fiber intake, a reduction equivalent to ~418 kJ/d (100 kcal/d) in these studies (92,93). This relationship appears to be dose dependent, as evidenced by manipulations of dietary fiber content leading to 150-kJ/d (36 kcal/d) increases in fecal energy content for each additional 5 g/d fiber consumed (94). Similar effects on energy availability appear to be achieved when dietary substitutions of WG for RG are made, but only if dietary fiber intake increases substantially. Substituting ≥350 g/d of coarse or finely ground wholemeal bread for mixed wheat bread resulted in a 21-g/d increase in dietary fiber intake and a 3% reduction in digestible energy (95). However, substituting 105 g/d milled WG for RG did not affect fecal energy excretion when dietary fiber intake increased by only 7 g/d (68). Similarly, an 84-g/d rolled oats intervention did not affect the fecal energy content of healthy adults despite a 4-g/d increase in soluble fiber intake (71). Taken together, these findings suggest that consuming WG-rich foods may contribute to body weight regulation, at least in the short term, by reducing energy availability, but only if substantial increases in dietary fiber intake are concurrent.

Glycemic response

By combination of reduced nutrient availability and delayed gastric emptying, viscous fibers reduce the postprandial glycemic response (90). Foods that elicit high glycemic responses are postulated to promote fat storage and hunger by augmenting postprandial insulin secretion and altering counter-regulatory hormone responses (96,97). However, the glycemic response associated with consuming WG foods is less dependent on the fiber content of the grain. Rather, factors such as the structural integrity, grain particle size after processing, and the food matrix appear to be the primary determinants of glycemic responses to WG foods (98).

Holt et al. (77) demonstrated progressive reductions in postprandial glycemic and insulminemic responses with increasing particle size following consumption of WG wheat provided in intact, cracked, coarse, and finely ground forms and similar findings have been reported for maize, barley, and rice (99–102). Appetite may also be affected by grain processing, as Holt et al. (77) documented higher satiety ratings following consumption of the intact relative to the finely ground grain. More recently, Kristensen et al. (103) measured glycemic responses and appetite following consumption of 4 separate meals composed of either bread or pasta made using milled WG wheat or refined wheat flours. No differences in energy intake at the subsequent meal were observed, though the WG bread was rated as more satiating that the RG wheat bread. Consuming WG foods had no effect on glycemic responses despite being higher in fiber, suggesting the relative importance of particle size and structural integrity. Further, glycemic responses were attenuated following consumption of the pastas compared with the...
breads, demonstrating the importance of the food matrix on glycemia (103).

In addition to postprandial modulation of glycemic responses, WG-rich meals have also been shown to favorably affect glucose metabolism following the subsequent meal (104), an occurrence termed the “second meal effect.” Nilsson et al. (105,106) recently extended this finding by demonstrating that, relative to RG wheat bread, consuming an equivalent amount of available carbohydrate from barley kernels prepared using various methods at evening meals depressed the glycemic response following a standardized breakfast the next morning. Colonic fermentation of indigestible carbohydrate was postulated to be an underlying mechanism as evidenced by inverse associations between glycemic responses and breath hydrogen, plasma SCFA, and plasma glucagon-like peptide-1 (GLP-1) concentrations (106,107). Similar effects, however, were not observed when wheat kernels were substituted for barley (105) or when the barley meal was consumed at breakfast and glycemic responses measured following the subsequent dinner 9.5 h later (108). In a separate study, compared with RG wheat bread, an evening meal consisting of barley kernels depressed the postprandial glycemic response, enhanced peripheral insulin sensitivity, and increased breath hydrogen and plasma butyrate concentrations the following morning (109). Of note, the fiber contents of the barley meals consumed in these studies exceeded the average daily amount consumed by Americans (110) and reached 81 g/meal (106). Thus, whether these findings are applicable to the types and amounts of WG commonly consumed is unclear.

Fermentation and the gut microbiota
The studies of Nilsson et al. (105–108) and Priebe et al. (109) draw attention to the potential influence of the gut microbiota in mediating relationships between WG intake and body weight regulation. SCFA produced during the fermentation of certain fibers within WG contribute to the regulation of body weight and composition by serving as metabolizable energy sources, directly mediating hepatic and peripheral glucose and lipid oxidation and stimulating secretion of the gut hormones peptide-YY and GLP-1, which act to suppress appetite, slow gastrointestinal transit, and modulate glucose metabolism (111). SCFA production is influenced by a number of factors, including the availability of fermentable substrate and the composition of the gut microbiota (112). Substrate availability and gut microbiota composition are interrelated, as evidenced by the prebiotic effect, a symbiotic relationship between the gut microbiota and human host whereby specific fermentable carbohydrate selectively promote the proliferation of colonic bacteria beneficial to host health (113). Emerging evidence has demonstrated that the composition of the gut microbiota may be linked to human obesity (114–120) and is sensitive to multiple dietary factors (116,121–124), thus suggesting a possible role for WG in body weight regulation via modulation of the gut microbiome.

Few studies to date have investigated interrelationships between WG-based diet interventions, gut microbiota composition, and energy regulation. Consuming 48 g/d of WG wheat (125) or maize (61) cereals over 3 wk was shown to have a prebiotic effect in 2 separate trials; however, similar effects were not observed when 150 g WG/d from a variety of food sources was consumed over 2 wk (66). The short duration of these studies precludes any meaningful conclusions with regard to body weight regulation from being reached, and only one study quantified energy intake, reporting no effect of the WG intervention (66). No changes in fasting insulin, fasting glucose, or fecal SCFA concentrations were reported in any of these studies, nor was breath hydrogen excretion or endocrine mediators of appetite such as peptide-YY or GLP-1 measured.

Inulin and oligofructose are prebiotic fibers found in a variety of cereal grains but predominantly obtained from wheat products in American diets (126,127). Daily oligofructose supplementation has been shown to alter glucose metabolism, enhance postprandial gut hormone responses, increase breath hydrogen levels, and promote weight and body fat loss, suggesting interrelationships between prebiotic fiber intake, gut microbiota activity, and energy regulation (128,129). However, these effects may be dose dependent, because similar effects are not always observed at lower doses (130). Though these studies provide some support for a beneficial effect of intrinsic WG components on body weight regulation, the amount of oligofructose shown to be effective (>16 g/d) would be difficult to consume from WG products alone (9), and more work is needed to determine if smaller doses achieved through consumption of WG would have similar beneficial effects.

Conclusion
Evidence for beneficial effects of WG intake on body weight regulation should derive from randomized controlled trials demonstrating spontaneous weight loss, enhanced weight loss during energy restriction, or prevention of weight (re) gain in response to increased WG intake. Recent trials examining the effects of substituting WG for RG on body weight regulation do not provide evidence for a benefit of WG consumption, which is counter to epidemiologic observations. However, the nature of WG interventions employed may have dampened the ability to detect effects of WG intake on body weight regulation. In particular, the <10-g/d differences in dietary fiber intake achieved by substituting WG for RG in these studies is less than what has been reported to induce even modest weight loss (131,132) and may have been insufficient to modulate short- or long-term mechanisms involved in body weight regulation. The differences in fiber intake achieved, however, are consistent with the increase in total daily fiber intake expected for an average individual adopting the 2010 Dietary Guidelines for Americans recommendation to replace RG with WG. Currently consumed forms of WG may also mitigate the potential benefit of WG consumption on body weight or composition. Processing clearly influences WG-mediated postprandial physiologic responses, with less...
processing associated with metabolic effects most likely to benefit body weight and composition, specifically the blunting of postprandial glycemic and insulinemic responses. Intervention trials commonly used commercially available or similar food products in which WG ingredients are more often processed and reconstituted than consumed intact. Although using these products reflects the current food environment, the null findings may suggest that many WG products, as commonly consumed, are ineffective for facilitating weight control or triggering the underlying physiologic mechanisms.

Reproducing recent findings of beneficial effects of WG intake on body composition and elucidating the underlying mechanisms should be targeted in future trials because central adiposity is a more clinically relevant predictor of metabolic risk than body weight or BMI (133). It is intriguing to speculate that the mechanisms derive from interactions between WG intake, gut microbiota composition, and host physiology. Direct effects of the gut microbiota on fatty acid metabolism and the regulation of total body and fat mass have been demonstrated (134,135); however, much of this work is restricted to animal and in vitro models, with the relevance to humans undetermined. Owing to recent advances in molecular biology techniques, the study of dietary influences on the human gut microbiome has become more accessible. Long-term randomized trials applying these techniques to explore interrelationships between WG-based diet interventions, gut microbiota composition, and the regulation of adiposity are needed.

In summary, intervention trials conducted to date have failed to demonstrate beneficial effects of WG intake on body weight regulation despite observational studies consistently demonstrating that high intakes of WG are associated with lower BMI, and the existence of a variety of mechanisms that could result in WG-mediated effects on body weight. Nonetheless, recent findings suggesting possible beneficial effects of WG intake on body composition deserve further attention. Investigations of sufficient duration to capture changes in body composition, providing less processed forms of WG, comparing different varieties of WG, and discriminating between effects of fiber and WG are needed. The continued development of biomarkers of WG intake is also needed for monitoring compliance in these studies. Plasma and urine alkylresorcinol concentrations are promising in this respect (66,68), though large interindividual variation; exclusivity to WG wheat, rye, barley, and triticale; short half-life; and possible nonlinear increases at high levels of WG intake remain limitations (136).

At present, insufficient evidence exists to demonstrate clear beneficial effects of WG intake on body weight regulation. However, given the nutritive superiority of WG relative to RG, WG consumption should continue to be encouraged as part of a health-promoting diet.

Acknowledgments
Both authors read and approved the final manuscript.

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