Perspective: Whole and Refined Grains and Health—Evidence Supporting “Make Half Your Grains Whole”

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ABSTRACT

Research-based dietary guidelines suggest that consumers “make half their grains whole.” Yet some advocate ingesting only whole-grain foods (WGFs) and avoiding all refined-grain foods (RGFs). Some even recommend avoiding all grain-based foods (GBFs). This article will provide arguments to counter negative deductions about GBFs and RGFs, especially staple ones, and to support dietary guidance recommending a balance of GBFs—achieved through the right mix, type, and quantity of WGFs and RGFs. Studies looking at early mortality, body weight, and glucose tolerance and diabetes will be used as examples to characterize the literature about GBFs. The following issues are highlighted: 1) inconsistent findings between epidemiological and interventional studies and impacts of GBFs on health outcomes, and the underreporting of findings showing RGFs neither raise nor lower health risks; 2) multiple confounding and potential interactions make adequate statistical adjustment difficult; 3) nonuniform WGF definitions among studies make comparison of results challenging, especially because some WGFs may contain 49–74% refined grain (RG); 4) binary categorization of GBFs creates bias because nearly all categories of WGFs are recommended, but nearly half the RGF categories are not; 5) ingestion of >5 (30-g) servings RGFs/d and <1 serving WGFs/d creates dietary imbalance; 6) pattern names (e.g., “white bread”) may impugn RGFs, when names such as “unbalanced” or “few fruits and vegetables” may more fairly characterize the dietary imbalance; 7) avoidance of all enriched RGFs may not only impair status of folate and other B vitamins and certain minerals such as iron and zinc but also decrease acceptability of WGFs; 8) extrapolation beyond median documented intakes in high-WGF consumers (∼48 g whole grain/d) in most cohorts is speculative; 9) recommended dietary patterns such as the Mediterranean diet demonstrate that the right mix of WGFs and RGFs contributes to positive health outcomes. Adv Nutr 2020;11:492–506.

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Introduction: The Need for Whole and Refined Grains in the Diet

Grain-based foods (GBFs) supply much of the world’s energy (E) and nutrient needs, providing 25–50% of E in Western diets and over half the world’s calories (1, 2). Moreover, they are important sources of carbohydrates and dietary fiber (DF). Dietary guidance around the world recommends 40–65% of E as carbohydrates, with 65% regarded as high by some (1–3).

GBFs also are important sources of micronutrients and plant-based protein. The protein, although incomplete, provides amino acids that complement those found in other plant foods (e.g., nuts and legumes) to make complete proteins, in foods that are affordable, shelf-stable, portable, versatile, and popular. GBFs will play a key role as the world transitions to plant-based diets to meet future food supply needs (1, 2).

Health promotion bodies worldwide recognize GBFs’ critical role in their food group–based recommendations. In pictorial food-based guidance such as USDA MyPlate or the Japanese Pagoda, GBFs are prominent in these culturally specific icons (1–10). The importance of GBFs, especially of whole-grain foods (WGFs), is being undermined by popular diets claiming these foods are unnecessary or unhealthful. Yet, diets that omit all GBFs will lack cereal fiber and may have inadequate intakes of micronutrients.

Dietary guidance since 2005 has underscored the importance of WGFs by specifically suggesting that “half of the
grains should be whole grains” (WGs) (4). The American Association of Cereal Chemists defined WGs as follows: “Whole grains shall consist of the intact, ground, cracked or flaked caryopsis, whose principal anatomical components— the starchy endosperm, germ and bran—are present in the same relative proportions as they exist in the intact caryopsis” (11). This definition was adopted by regulatory and health promotion bodies in order to encourage consumers to replace some refined-grain foods (RGFs) with WGFs (7–10, 12–14).

Refined grains (RGs) differ from WGs in that some or all of the outer bran layers are removed by milling, pearling, polishing, or de-germing. These processes reduce micronutrients, decrease DF by ≤75%, and lower some antinutritional components held in the bran (2). Refined, enriched grains (REGs) have micronutrients added to replace some of these losses. In some jurisdictions, RGs may be subject to mandatory or voluntary fortification of folate and other micronutrients.

Health impacts of WG ingestion have been the focus of epidemiological analyses, randomized controlled trials (RCTs), reviews, and meta-analyses for the last 20 y (15–101). Epidemiological studies and their meta-analyses consistently show those in the quintile ingesting the highest quantity of WGFs, compared with those in the quintile eating the lowest, are associated with lower risks of overall or cause-specific early mortality and chronic diseases (17–32). Specifically, WGFs are associated with reduced risks of obesity or overweight (33–62); abnormal glucose tolerance, prediabetes, and type 2 diabetes (T2D) (41, 50, 62–77); elevated inflammatory markers (41, 77–79); blood pressure (80, 81); or blood lipids; and certain cancers (88–94). Such consistency is not observed in results from RCTs (51–61, 71, 79, 95–101).

The health impacts associated with RGFs are often reported in the same studies looking at WGFs; however, the results are less widely promulgated. Whereas numerous reviews focus on WGFs, few focus on RGFs. Those that do show a null effect or associations with slightly lower health risks for many health outcomes (102, 103). Such findings support recommendations for “half the grains to be whole” (4–6).

Although some research shows increased risks associated with RGFs and metabolic syndrome, T2D, and biomarkers such as blood glucose or lipids (56–67, 75), the adverse impacts are not seen consistently. They are more likely in the following scenarios: 1) total calories or number of grain servings exceed E needs; 2) total carbohydrate intakes are >60% of E; 3) RGFs are mostly nonrecommended, indulgent ones; and 4) persons at risk of certain conditions may benefit from lower carbohydrate intakes (40–45% of E) (3).

USD A data covering the period 1970–2010 document increasing intakes of GBFs and percentage of E from carbohydrate (104). These increases correlate with increasing rates of obesity over the same time period and are used by some to posit that GBFs and carbohydrates are the cause of obesity and chronic disease. However, the correlations do not prove causation, and during that same time period available E from most food groups increased, a more likely cause of weight gain and associated chronic disease risks (104). In addition, the correlation was no longer relevant after 2010 because GBF intake decreased, but obesity continued to rise (105).

Negativity concerning and blaming carbohydrates and GBFs, especially RGFs, continue (106–114). Many deduce that positive impacts for ingestion of WGFs imply negative ones for RGFs and recommend limitation or elimination of RGFs by promoting Paleo, ketogenic, very-low-carbohydrate diets or advocating for ingestion of WGFs only (106–114). RGFs were denounced by one researcher as “the single most harmful influence in the American diet today” (107).

The popular press and public health professionals tout positive findings about WGs but ignore or fail to fully report null findings on RGFs. Such pronouncements color perceptions of RGFs, as demonstrated in a 2018 survey (115): 80% of respondents believed WGFs were “healthy,” compared with 40% for RGFs, and 15% named RGFs “unhealthy.”

In-depth discussion of data for 3 health endpoints will serve as examples for 9 arguments to support the current dietary recommendations “to make half your grains whole” (4, 5, 6). Further, the documented benefits associated with ingestion of WGFs will be discussed together with a number of issues that inadvertently bias findings against RGFs.

WGFs are consistently associated with improved health outcomes in epidemiological studies, but not in RCTs; RGFs are not associated with risks in many of the same studies

Ingestion of 48 g WGs/d (~2.7 one-ounce (30-g) WGF servings/d) is consistently associated with health benefits in prospective cohort and case-control studies and their meta-analyses. No such consistency is observed in results from RCTs and their meta-analyses, even when all WGFs are fed (15–101). RGFs, in many of the same epidemiological studies
finding benefits of WGFs, often show a null effect, or even a risk-lowering effect. Such findings may not be emphasized or communicated (116–119). Three health outcomes—risk of early mortality, risk of elevated body weight, and risk of elevated glycemia and T2D—will show how epidemiological findings on GBFs differ from those observed with RCTs and are indicative of a variability observed for most health outcomes.

Studies of WGs and RGs have multiple sources of confounding
Better health outcomes and lower disease risks are associated with WGF ingestion, but clear attribution to WGFs is difficult because high-WG eaters have lifestyles and diets deemed healthier, and vice versa (32, 37, 44, 49). The multiple confounding and potential interactions call into question the adequacy of multiple statistical adjustments (118).

WGF and RGF definitions are inconsistently applied and may be a source of error
Nonuniform definitions of and criteria for determining WGFs, together with imprecise terms for data collection (e.g., dark bread), or mis-categorization of foods, such as dark bread, bran, couscous, or crackers, can affect results and make comparisons among studies difficult (31, 32, 37, 44, 65, 120–124).

Binary categorization of GBFs into RGFs and WGFs
Early epidemiological studies classed foods as either WG or RG (31, 32). This was continued in most subsequent studies. Inadvertent bias against RGFs may have occurred because nearly all WGFs are recommended, staple GBFs, but over half of RGFs’ calories come from nonrecommended, indulgent GBFs. No study has yet been published that compares health outcomes of staple and nonstaple WGFs and RGFs.

Intakes of GBFs are unbalanced
Consumers worldwide fail to meet the recommended balance of GBFs, e.g., for a 2000-kcal diet, six 30-g servings of GBFs, with half being WGFs. WGFs are underconsumed, and RGs are overconsumed through large portions, more servings than recommended, and frequent ingestion of indulgent, nonrecommended RGs (4, 6, 39, 124–131). When carbohydrate intakes approach 65% of E, overconsumption of RGs, especially when diet quality is marginal or a person has certain metabolic conditions, may increase health risks (3, 69, 70).

Named patterns (e.g., “white bread”) may be a source of inadvertent bias
Named dietary patterns, such as “white bread” (38), may promote deductions that the named food, not the pattern, is associated with health risks.

Recommendations for all WGFs may lower WG consumption and nutrient status
Foods formulated with both RGs (especially REGs) and WGs not only improve acceptability of WGFs, especially for children (132, 133), but also improve micronutrient content and/or availability and reduce intake of antinutritional components found in bran (134–138).

Recommendations for only WGFs extrapolate beyond existing data
Most epidemiological studies show health benefits of three 30-g WGF servings/d (48 g WG/d). Higher intakes are documented in regions such as Scandinavia, where the mix of grains includes a significant proportion of wheat, rye, barley, and oats. However, extrapolations using these data may have limited applicability in other regions.

Dietary pattern research supports the right mix of RGs and WGs
Recommended dietary patterns, such as the Mediterranean Diet (MEdiet), are associated with multiple positive health outcomes. These diet patterns demonstrate the health-promoting role of staple GBFs eaten in the recommended balance—half WGFs and half RGs.

These points will be discussed to support current recommendations of dietary guidance for “half the grains to be WGs.” Further, this discussion might spur reanalysis of existing studies, in which health impacts of indulgent GBFs are compared with staple GBFs. Such an analysis would have 4, not 2, GBF categories: WG staples, RG staples, WG indulgent foods, and RG indulgent foods.

Results and Discussion

WGFs are consistently associated with improved health outcomes in epidemiological, but not intervention, studies; RGFs may not be associated with increased health risks for some outcomes
High intakes of WGFs by consumers from different populations with diverse dietary intakes in epidemiological studies are consistently associated with lower total and disease-specific risk of early mortality (indicating a lower risk of dying during the follow-up period in prospective studies), improved measures of body weight, and lower risks of many chronic conditions. Despite a range of search strategies, databases, and inclusion criteria in meta-analyses of epidemiological studies, risk reductions consistently range from 10% to 25% for most health endpoints (15–50, 62–94). However, no such consistency was observed in RCTs and their meta-analyses (51–61, 95–101).

Mortality and GBFs.
Those ingesting the most WGFs were associated in prospective studies with lower RRs of mortality from all causes. Among studies, risk reductions of ≥15% were observed for those in the quintile ingesting the most WGFs (~3 servings/d) compared with the least (<1 serving/d).
RRs ranged from 0.78 (95% CI: 0.67, 0.91) to 0.85 (95% CI: 0.80, 0.91) (17–32). There were 17–30% decreases in risks across studies for death from cardiovascular or coronary disease (RR: 0.70; 95% CI: 0.61, 0.79 to RR: 0.83; 95% CI: 0.79, 0.86). There was a 6–18% range in reduction in cancer risks for high-WGF consumers (RR: 0.82; 95% CI: 0.69, 0.96 and RR: 0.94; 95% CI: 0.87, 1.01 per 90 g WG/d; P-heterogeneity < 0.001) (17–27).

Often the same studies that show inverse associations between early mortality and intake of WGs also assessed health impacts of RG intake (18, 24–26, 29–32). Daily consumption of 6–7 servings (180–210 g/d) of RGFs did not raise mortality risk (RR: 1.02; 95% CI: 0.26, 1.45; P-heterogeneity = 0.64) (31). The same is true of GBFs, e.g., total bread (RR: 0.77; 95% CI: 0.72, 0.81; P-heterogeneity = 0.42) and breakfast cereals (RR: 0.87; 95% CI: 0.81, 0.93; P-heterogeneity = 0.17) (31, 102, 103). There was a wide range of RRs: 0.82 (95% CI: 0.48, 1.40) to 1.46 (95% CI: 0.80, 2.67). One meta-analysis (18) showed half the studies on RGfs had RRs <1.02 and 16 of 19 had RRs <1.11. Thus, RGs were not associated with increased risk of early mortality from heart disease (RR: 1.16; 95% CI: 0.84, 1.59; P-heterogeneity = 0.12). Neither were white bread (RR: 1.07; 95% CI: 0.86, 1.34; P-heterogeneity = 0.160) nor total rice (RR: 0.98; 95% CI: 0.90, 1.07; P-heterogeneity = 0.44) (18). However, there was a possible trend toward increased risk for refined breakfast cereals (RR: 1.15; 95% CI: 0.79, 1.67; P-heterogeneity = 0.07) (18). Williams (103) and Williams et al. (47) reported similar findings for RGs but did not document an increased risk associated with breakfast cereals. Differences in background diets, total RG intakes, definitions of WGFs, and adjustment for various confounders may all contribute to variability of outcomes.

**WGns and body weight: epidemiological studies.**

WG consumption, in a variety of cross-sectional and prospective studies (33–50), is associated with lower risks of obesity measures such as high waist circumference (WC), visceral adipose tissue (VAT), BMI (in kg/m²), and fat mass. In most studies the risk was ~15% lower for high-WG consumers. Weight gain, over 8-y follow-up, was significantly lower (0.75 kg compared with 1.24 ± 0.23 kg, P-trend < 0.0001) for men ingesting a mean of three 30-g WGF servings/d (42.7 g WG/d) than for those eating very little WG (<5 g/d) (34). A meta-analysis of 13 prospective studies found that WG intake was associated with lower weight gain, ranging from 0.4 to 1.5 kg, during 8–13 y of follow-up (50).

In the Framingham Heart Study (35), there was an inverse relation of WGF intake with VAT and WC (P-trend < 0.001). Although increased RGF consumption was associated with increased VAT and WC (P-trends < 0.001) (35), the lowest VAT was observed with 2 servings of RGfs and 3 of WGFs, a balance approximating “half the grains as whole grains.”

Cross-sectional data from NHANES 2001–2012 also showed a significant inverse relation of WG intake with BMI and overweight or obesity (39, 40). For example, the mean BMI ± SD for adults who ate no WGFs was 28 ± 0.1 compared with 27.6 ± 0.1 (P < 0.0001) for those who ate ≥1 WGF serving (39).

Low grades were assigned to the strength of the epidemiological evidence. Cho et al. (44) gave a grade of “C/D” owing to inconsistent results or methodological flaws. Further, reanalysis showed that only the inclusion of bran foods as WGFs resulted in a significant association. Schlesinger et al. (49) observed a weak inverse association between WGF intake and overweight/obesity (RR: 0.93; 95% CI: 0.89, 0.96) but graded the dose–response as “very low to low quality.”

Results from RCTs studying WGFs and measures of weight are variable (50–61). Compared with RGfs, WGFs did not result in significant differences in weight or weight loss in a meta-analysis of 26 studies (weighted difference: 0.06 kg; 95% CI: −0.09, 0.20 kg; P = 0.45) (51). Similarly, no significant differences in BMI, fat mass, or fat-free mass were observed in 21 RCTs, even 1 with large numbers of subjects (52, 53). Nor were there any significant effects with regard to body fat percentage [weighted mean difference (WMD): 0.27%; 95% CI: −0.05%, 0.58%; P = 0.09], fat mass (WMD: 0.45 kg; 95% CI: −0.12, 1.02 kg; P = 0.12), or WC (WMD: 0.06 cm; 95% CI: −0.50, 0.63 cm; P = 0.82) (53). Several studies showed that weight was lost with both WGs and RGs (54–56); a slightly lower body fat percentage (weighted difference: −0.48%; 95% CI: −0.95%, 0.01%; P = 0.04) was observed with WGFs in 1 study (51). In another study where 33 low-WG consumers substituted WGFs for RGfs, there was a trend toward lower body weights but differences did not reach statistical significance (Δ intervention 2-sample t test, P = 0.10), as for BMI (Δ intervention 2-sample t test, P = 0.08) (55).

Greater consistency was seen among studies where subjects had high intakes of WGs, especially when WG rye or oats were eaten (57–60). In a 1-y study of 298 subjects with T2D, a healthy diet plus 100 g/d of WG oats promoted −0.89 kg (95% CI: −1.56, 0.22 kg) greater mean weight loss than occurred with the usual-care high-fiber, low-fat diet (57). In another study, addition of ready-to-eat cereal (RTEC) WG oat cereal with 3 g β-glucan to intervention diets did not result in a significant difference in weight loss from the control (−2.2 ± 0.3 compared with −1.7 ± 0.3 kg, P = 0.325), but did significantly decrease WC (−0.3 ± 0.4 compared with −1.9 ± 0.4 cm, P = 0.012) (58). In an 8-wk crossover study, 59 Danes ate either 179 ± 50 g WGFs/d or <13 g WGFs/d. The very high WG intake resulted in −0.2 kg loss compared with a 0.9-kg gain (P < 0.001) for those eating mostly RGs (59). Fat-free mass was lower (P = 0.010), and there was a tendency for lower WC (P = 0.097) (59). A 6-wk intervention comparing wheat and rye found that, compared with RG wheat, WG rye caused greater mean loss of body weight (+0.15 ± 1.28 and −1.06 ± 1.60 kg, respectively, P < 0.01) and fat mass (−0.04 ± 0.82 and −0.75 ± 1.29 kg, respectively; P < 0.05) (60).

Many RCTs replaced RGfs with WGFs in diets of consumers with habitually low WG intake. However, many showed little effect on weight. Calorie restriction had larger impact than WG or RG (61). A few RCTs, usually with grains
such as rye or oats, showed trends toward reductions in some measures of weight. Although mechanisms of action have been suggested, the losses of <5% body weight found in most studies raise questions about clinical or health relevance (139).

**RGs and body weight.**

Findings on RGFs and body weight are also not consistent. Some large cohort studies show that intake of RGFs is associated with increased risk of weight gain or higher BMIs. However, this usually occurs with intakes of RGFs higher than recommended. For example, analysis of food frequencies of middle-aged female nurses shows RG median intakes for the highest and lowest quintiles were 2.77 servings \(\cdot 1000 \text{kcal}^{-1} \cdot \text{d}^{-1}\) and 0.40 servings \(\cdot 1000 \text{kcal}^{-1} \cdot \text{d}^{-1}\), respectively. Thus, at 2000 kcal/d those at the highest intakes would be ingesting >5 grain servings daily. Thus, the chances of BMI > 30 were elevated (adjusted OR: 1.18; 95% CI: 1.01, 1.35; \(P\)-trend < 0.0001) (45). However, the ORs for quintiles 2–4 hovered around 1.0 (OR: 0.96; 95% CI: 0.88, 1.05; OR: 0.94; 95% CI: 0.86, 1.00; and OR: 1.03; 95% CI: 0.95, 1.13, respectively; \(P\)-trend < 0.0001) (45). In contrast, dietary records from the Baltimore Longitudinal Study on Aging showed median RG intake of 39 g/d in the lowest quintile and 102 g/d in the highest quintile. Neither mean baseline BMIs ± SD for those in the lowest quintile of refined grain intake compared to the highest quintile of intake (24.9 ± 0.2 vs 25.2 ± 0.2, \(P = 0.51\), respectively) nor body weights ± SD (73.5 ± 0.7 vs 73.9 ± 0.7 kg, \(P = 0.78\), respectively) were significantly different (38). In a meta-analysis of food groups (49), a J-shaped risk curve with increasing intakes of RGFs was observed (\(P\)-nonlinearity < 0.001). The RR of elevated body weight was <1 for RGF intakes between 0 and 90 g/d but increased with intakes of >100 g/d. At intakes of 200 g/d, the RR increased to 1.43 (95% CI: 1.26, 1.63).

Daily ingestion of breakfast cereals, in any combination of WG and RG, compared with infrequent ingestion (≤1/wk) by men in the Physicians’ Health Study was associated with greater likelihood of having a BMI < 25 (RR: 0.81; 95% CI: 0.64, 1.03; \(P\)-trend < 0.03) (43). This association was assigned a “grade of B” (140).

The effect of RG intake on weight gain lacks consistency. White bread consumption for those students in the Seguimiento Universidad de Navarra (SUN) cohort in the highest quartile of intake (median ± SD) (171 ± 62 g/d; 6 slices per day), compared with the quartile with the lowest intake (<3 ± 4 g/d; <3 slices per week), was associated with an elevated risk of becoming overweight or obese (adjusted OR: 1.40; 95% CI: 1.08, 1.81; \(P\)-trend = 0.008) (46). While a significantly elevated risk was observed for those with the highest intakes, the ORs for the 2 middle quartiles were only slightly elevated. For those in the second and third quartiles, white bread intakes were 36 ± 11 g/wk and 60 ± 0 g/d (420 ± 0 g/wk), but the adjusted ORs were similar (OR: 1.14; 95% CI: 0.90, 1.50 and OR: 1.12; 95% CI: 0.90, 1.50, respectively). If white bread is associated with elevated body weight, it is illogical that a mean consumption of 380 g/wk more white bread caused no difference in the risk of overweight in the middle quartiles.

Such data may be explained by significant confounding. Students in the SUN quartile with the highest white bread intake also had higher baseline BMIs and body weights and significant differences in the 21 dietary qualities measured, with most varying in ways considered less healthful (\(P < 0.0001\)). With significant dietary differences including a mean of 446 more calories per day for white-bread consumers (\(P < 0.001\)), adverse health outcomes ascribed to white bread intake may be misleading (46).

The impact of RGFs on weight depends on overall diet and total grain intake. Chinese adults eating >401 g white rice/d, compared with <200 g/d, were associated with less weight gain in 5 y (–2.08 kg; 95% CI: –2.75, –1.41 kg; \(P < 0.001\)) (141). These findings should not be interpreted to mean that high rice consumption does not provide more calories, but rather to emphasize that total calories and other food choices, not rice alone, determine weight gain.

Low grades were assigned to the quality of the data on RGFs and weight. In a meta-analysis of food groups, those eating the highest compared with the lowest number of RGF servings per day had a greater risk of weight gain (RR: 1.18; 95% CI: 0.95, 1.50), but the NutriGrade quality of evidence was graded “very low” (49). Further, risk of weight gain was flat until consumers ate ≥3 servings/d (49). The German Nutrition Society’s evidence-based review on carbohydrates and other reviews concluded there was insufficient evidence to link RGFs to weight, obesity, and most measures of body fatness (142). In cases where evidence exists, it was deemed weak and effects null or small and significantly confounded (49–51, 53, 102, 103).

**WGs, glycemia, and diabetes.**

Ingestion of WGFs (~3 servings/d) was associated, in a number of prospective cohort studies and systematic reviews, with decreased risks of incidence of and mortality from T2D (15–28, 62–72). In meta-analyses Aune et al. (18, 68) found that 3 WGF servings/d were associated with a reduced risk of T2D and death from T2D (summary RR: 0.68; 95% CI: 0.58, 0.81; \(I^2 = 82\%\); and RR: 0.49; 95% CI: 0.23, 1.05; \(P\)-nonlinearity < 0.0001, respectively). Similar risk reductions were reported in other studies for T2D and associated biomarkers such as glucose tolerance or inflammation and for intakes of specific WGFs including breads, cereals, rye, oats, and rice (50, 63–77).

In a meta-analysis assessing the impact of food groups on T2D risk, WGFs reduced the risk (RR: 0.77; 95% CI: 0.71, 0.84) (76). The strength of association was graded “high,” with the greatest risk reduction occurring with WG intakes between 0 to 40 g/d (76). Similarly, Aune et al. (68) drew a U-shaped curve, suggesting the lowest risk occurs with ~3 WGF servings/d (50 g/d).

Confounding by DF and by other variables known to lower diabetes risk makes attribution of risk to WGs alone challenging. Those in the Women’s Health Initiative (WHI) who ingested >2 WGF servings/d had a reduced risk of
T2D (HR: 0.75; 95% CI: 0.63, 0.89; \( P < 0.0139 \)) (62).

When adjusted for lifestyle and most dietary factors, the association remained; however, adjustment for DF attenuated it. A similar attenuation was observed when bran foods were not counted as part of WGFs (44, 65).

Lower incidence of T2D is associated in epidemiological studies with habitual consumption of \( \sim 3 \) WGF servings/d (50 g WG/d). Calls for higher WG intake are speculative because only a few cohorts consume higher amounts. In Scandinavia the highest quintile of WG intake reaches \( 170 \) g/d and includes a variety of WGFs: oats, barley, and rye. Each is associated with lowering inflammation and blood sugar parameters (64). Extrapolations for intakes beyond 50 g/d WG may not apply to all populations (67) where lower intakes are documented and WG mixtures differ.

**RGFs, glycemia, and diabetes.**

Many studies showing that WGFs reduce T2D risk also find that RGFs, especially in Western cohorts, do not increase, and may even lower, risk (18, 65–77). In a meta-analysis of 15 prospective studies assessing RGFs and T2D, the range of RGF intake was 0–700 g/d and the risk of T2D for the highest compared with the lowest quintile was not elevated (RR: 1.01; 95% CI: 0.92, 1.10) (76). Similarly, a recent meta-analysis of 16 cohort studies found RGF intake was not associated with risk of T2D (RR: 0.95; 95% CI: 0.88, 1.04) (68). Women in the WHI eating \( \geq 6 \) RGF servings/d compared with \(<1\) serving/d had a lower risk of T2D (adjusted HR: 0.73; 95% CI: 0.60, 0.87; \( P < 0.0519 \)) (62). However, RGFs were positively associated with fasting insulin (P-trend = 0.002) in women in the Baltimore Longitudinal Study of Aging (37).

RGFs were associated with increased risk of T2D in regions with high intakes of carbohydrate and/or rice \((\geq 200 \text{ g/d})\) (141, 143–152). In parts of India where carbohydrate intakes for the highest quartiles are above recommendations at \( >72.8\)% of E and DF intakes low and mean intake \( \pm \) SD of RGFs was 516.5 \( \pm \) 137.1 g/d, the risk of T2D for those in the highest quartiles of intake was markedly increased (adjusted OR: 4.98; 95% CI: 2.69, 9.19; \( P < 0.001 \)) (143, 144). The quartile ingesting median white rice intake of 587 g/d, compared with those ingesting less, had elevated T2D risk (OR: 5.31; 95% CI: 2.98, 9.45; \( P < 0.001 \)) (143, 144). For Chinese middle-aged women with high carbohydrate and white rice \((\geq 200 \text{ g/d})\) intakes, T2D risks were raised but not nearly as much as in India (RR carbohydrate: 1.28; 95% CI: 1.09, 1.50; RR rice: 1.78; 95% CI: 1.48, 2.15) (141). In the Japan Public Health Center-based Prospective Study, white rice intake was associated with T2D in women (OR: 1.65; 95% CI: 1.06, 2.57; P-trend < 0.005, for the highest compared with the lowest quartile) (145, 146). There was a nonsignificant trend in sedentary men (P-trend = 0.08) (146). However, these same data analyzed by dietary patterns showed that in those eating the “westernized breakfast pattern” with more bread and less rice, RG intake was inversely related to A1C concentrations (P-trend = 0.02) (147). In the Chinese Jiangsu study, hyperglycemia risk increased linearly as rice intakes increased across tertiles from \(<200\) to 201–400 and \( \geq 401 \text{ g/d} \) (RR: 1; 1.96; 95% CI: 1.07, 3.60 and RR: 2.50; 95% CI: 1.37, 4.57, respectively; \( P\)-trend < 0.005) (147).

Carbohydrates provided 57.7% of E in urban Tehran and 56.9% of E in rural Iran (Golestan). However, mean total calorie intake was also roughly 200 calories/d more in Tehran than rural Iran. Rice intake impacted T2D risk not only because of differences in caloric intake, but also perhaps because the mean rice intake is 250 g/d and 15.7% of E in urban Tehran and 120 g/d (77–210 g/d) and 8% of E in rural Iranians. In Tehran those eating \( >250 \text{ g/d} \) of rice were associated with increased risk (adjusted OR: 2.08; 95% CI: 1.08, 3.91) compared with those eating less. In the rural cohort where white rice intakes are lower, there was a slightly increased risk for those in the tertil ingesting \( >210 \text{ g/d} \) of white rice (adjusted OR: 1.05; 95% CI: 0.85, 1.30; \( P < 0.001 \)) (148). Differences in lifestyle and diet in rural Iran including more activity, ingestion of more bread including soluble fiber and magnesium and less meat are postulated as attenuating T2D risk (148).

High rice consumption in other cohorts is not always associated with increased T2D risk. In the Singapore Chinese Cohort Study, there was no elevation of T2D risk due to high rice consumption. The median rice intakes for the high and low quintiles varied from 236.5 to 649.3 g/d with the adjusted HR: 0.98; CI: 0.90, 1.08) (149). However, this study differs from others because risk calculations were adjusted for many factors and shows that other foods such as meat or Asian noodles substituted for white rice increases the HR.

In a country where rice consumption is lower, its consumption was associated with reducing T2D risk. In a prospective cohort in southern Spain, “frequent” rice consumption (3 times/wk) versus less than once a week was associated with a lower risk of developing T2D over a 6-yr period (adjusted OR: 0.43; \( P = 0.04 \)) (150).

Meta-analyses do not help clarify matters. One comparing 3 Asian and 4 Western cohorts done in 2012 found an association between high rice intake and increased T2D risk (RR: 1.55; 95% CI: 1.20, 2.01; and RR: 1.12; 95% CI: 0.94, 1.33, respectively) (151). However, a 2017 meta-analysis of 11 studies found white rice consumption was not associated with increased risk of developing T2D (pooled RR: 1.08; 95% CI: 0.87, 1.33; \( P = 0.33 \), even when stratified by region for rice consumption (152).

Heterogeneity among studies is contributed by differences in genetics, lifestyle, and diet including rice intakes. For example, rice intakes in 3 US cohorts varied from 5.3 to 112.9 g/d across the quintiles (151). In Japanese cohorts, they ranged from 278 to 560 g/d, but in Shanghai women from 500 to 750 g/d with 67.5% of E from carbohydrate (82, 141, 145, 146).

Assessment of RGFs’ impact on T2D risk in RCTs requires the use of biomarkers such as blood glucose and insulin resistance (50–61, 79, 96–103), and they also show variability. Neither RGs nor WGs in a 6-wk crossover study (\( n = 33 \)) caused any difference in blood glucose values (\( \Delta \text{Glucose from baseline with RG intervention} 0.0 \pm 0.1 \text{ mmol/L and WG intervention:} -0.1 \pm 0.1 \text{ mmol/L; NS} \))
Meta-analyses of RCTs reflect the variation observed. One study of 21 RCTs showed significantly lower mean fasting glucose differences (−0.93 mmol/L; 95% CI: −1.65, −0.21 mmol/L; P-heterogeneity < 0.05) (50). Another showed that WGFs reduced the postprandial values of the glucose integrated AUC (iAUC) (0–120 min) by −29.71 mmol/L · min (95% CI: −43.57, −15.85 mmol/L · min; P = 0.477) in a meta-analysis of 20 studies (96). Similarly, ground WG and RG rye flours caused no difference in blood glucose curves iAUC (−5.5 mmol/L · min; 95% CI: −24.8, 13.8 mmol/L · min; P = 0.576). However, brown rice kernels, compared with white rice, resulted in a significant reduction in blood glucose response (iAUC: −6.7 mmol/L · min; 95% CI: −25.1, 11.7 mmol/L · min; P = 0.477) in a meta-analysis of 20 studies (96). The degree of grinding/milling had an impact on blood glucose. Consumption of foods from either WG or RG wheat flour did not cause a significant reduction in blood glucose (iAUC: −6.7 mmol/L · min; 95% CI: −25.1, 11.7 mmol/L · min; P = 0.477) in a meta-analysis of 20 studies (96). Similarly, ground WG and RG rye flours caused no difference in blood glucose responses (iAUC: −5.5 mmol/L · min; 95% CI: −24.8, 13.8 mmol/L · min; P = 0.576). However, brown rice kernels, compared with white rice, resulted in a significant reduction in blood glucose response (iAUC: −6.7 mmol/L · min; 95% CI: −25.1, 11.7 mmol/L · min; P = 0.477) in a meta-analysis of 20 studies (96).

Data on body weight and T2D show the variability seen with most health endpoints. WG ingestion may be associated with reduced risks in epidemiological studies, but findings are not consistent among studies. Confounding is a huge concern.

Because changes in biomarkers are measured, and not disease incidence, comparison of findings from RCTs and epidemiological studies is difficult. It is further complicated by varying designs, small numbers of subjects and their selection criteria, and the short duration of studies (<4 mo). Many factors appear to affect observed health outcomes in both types of studies including design, power, subject characteristics, compliance, background diet, grain type, WG definition used, and the type and mix of WGs.

Studies of WGs and RGs have multiple sources of confounding

Better health outcomes and lower disease risks are associated with ingestion of WGFs. In nearly all studies WGF consumers are documented as having health-promoting diets and lifestyles and vice versa (28, 31, 33–41, 44–46, 49). Specifically, WG consumers compared with RG consumers have higher Healthy Eating Indexes (HEIs), ingest less total E, sugar, alcohol, fat, red meat, and indulgent GBFs, and ingest more fruits, vegetables, and fish (41, 46, 91, 153).

Dietary variables covary. High intakes of RGFs, especially at amounts higher than dietary guidance, result in lower consumption of other recommended foods. For example, in the SUN cohort, as white bread consumption increased, vegetable and fruit consumption decreased (46, 153). This forces the question of whether observed associations are due to higher white bread intake, lower intake of fruits and vegetables, or their interaction.

Dietary choices also vary with lifestyle (153–161). High-WG consumers are more likely to have normal BMIs, higher educational attainment, and socioeconomic status, and to be physically active and nonsmokers, and vice versa (31, 32, 37, 46, 152–159, 162). Models attempt to adjust for many factors: calories, red and processed meat, fruits, vegetables, dairy, fat, protein, sugar-sweetened beverages (SSBs), antioxidants, nutrients, DF, measures of diet quality (e.g., HEI), relevant health history, baseline values (e.g., blood glucose or BMI), race-ethnicity, physical activity, smoking status, education, supplement and alcohol use, and menopausal status and hormone use. Because few adjust for all of the possible known confounders, the likelihood of residual confounding is substantial. The myriad of potential interactions may muddle accurate statistical adjustment, especially as factors tend to cluster, thus amplifying observed positive or negative effects (118).

Definitions of WGFs and RGFs are inconsistent and may be a source of error or bias

There is concurrence regarding the definition of WGs as an ingredient or single food (e.g., brown rice) (11–14), but little agreement regarding the definition of WGFs or ways to report WG intake (120–123). The varying definitions and criteria among studies make comparing results difficult. A few studies report grams of WG, which recognizes foods contributing any amount of WG. Most studies use ≥25% WGs/serving as initiated by Jacobs et al. (31, 32). With this criterion WGFs could contain 74% RG. A few studies use the FDA Health Claim of ≥51% WG by weight per serving (37, 123), which means WGFs could have 49% RG. These sharp cutoffs mean that foods with 24% or 50% WGs, respectively, are counted as RGFs. Because many WGFs may contain between 49% and 74% RG, the benefits attributed to WGFs may more accurately be associated with the mix of WGs and RGs.

Imprecise terms used in food frequencies coupled with consumers’ inability to identify WGFs or RGFs create error (160, 161, 163–165). For example, respondents are asked how frequently they eat “dark bread.” Caramel-colored or multigrain bread may be identified by consumers as “dark” despite it being mostly RGs. Conversely, light-colored RGFs made with white WG wheat may be classified as RG despite their WG content.

Mis-categorization errors also occur. Couscous, bulgur, farro, and barley were counted as WGFs, despite many marketplace forms being RG (31, 32, 164). Foods with 25% bran were deemed WG in some studies. Reanalyses excluding bran foods erased the significant risk reductions attributed to WGs (44, 65).

Foods with positive health images, e.g., WGFs, are more likely to be reported, whereas those with negative health images, e.g., indulgent RGFs such as sweets and cakes, are...
underreported, especially by overweight individuals (166, 167). This could create errors for both WG and RG intake data.

**Binary categorization into RGFs and WGFs**

Categorizing GBFs as either WGFs or RGFs (31, 32) inadvertently biases in favor of WGFs. Seven of 8 WGF subcategories are staple (core) foods recommended in dietary guidance (Table 1). Only the “popcorn” category might be indulgent. Assuming all popcorn is indulgent, then 87% of weekly intake WGFs in the Iowa Women’s Health Study (IWHS) are foods that contribute little sugar or fat and are recommended in dietary guidance. In contrast, RG food categories contain a mix of recommended and nonrecommended foods (3–8). Breads comprise 30% of the IWHS weekly RGF servings (31, 32). The addition of rolls, bagels, English muffins, pasta, pizza crust, rice, and RG breakfast cereals means that 46.0% of weekly RGF servings are recommended in dietary guidance. In contrast, 45.2% of the weekly RGF servings were “sweets and desserts.” With the addition of biscuits, muffins, pancakes, and doughnuts, over half the weekly intake of RG servings are foods that dietary guidance suggests “to limit” owing to contributions of added sugar, fat, and calories (Table 1) (31, 32).

**Intakes of GBFs are unbalanced**

Consumers worldwide under-consume WGFs and over-consume RGFs (5–10, 39, 124–129). Many consumers ingest more total grain servings than recommended for E needs (e.g., six 30-g servings per 2000 kcal) (5, 6). Many ingest little if any WG, creating an imbalance. Large portions and energy-dense, nonrecommended RGFs contribute to imbalance (131, 132). In the IWHS, those with the highest intake of RGFs had a median intake of all GBFs of 30 servings/wk (range: 23.0–155.5 servings/wk) including “grain-based sweets and desserts” (range: 11.5–143 servings/wk) (31, 32). In contrast, those with the highest intake of WGFs had a median intake of all GBFs of 22.5 servings/wk (range: 18.5–84.5 servings/wk). Such data confirm those eating the most RGFs ate more total GBFs with many being nonrecommended. High-RGF consumers had higher mean sugar intakes (47.8 g/d compared with 38.8 g/d) and more total E (9.7 MJ/d compared with 8.6 MJ/d) than high-WGF consumers (P < 0.001) (31, 32).

As demonstrated in previous sections, health risks associated with GBFs are exacerbated when diet quality is marginal, RG intake is high, WG and DF intakes are low, and carbohydrate intakes are near or above the recommended 65% of E (3, 141, 143, 144, 147, 148).

**Named patterns (e.g., “white bread pattern”) may be a source of inadvertent bias**

Dietary pattern research can yield insights beyond studies of single foods or components, partly because of the ability to assess dietary components that vary together (153–160). Patterns such as “white bread” or “RG and red meat” in epidemiological research are often associated with adverse health outcomes. Those not understanding pattern research as “a way of conceptualizing numerous diet exposures” (168, 169, may deduce that foods in the pattern name, not the pattern, are associated with increased risk (38). In reality, the pattern name describes diets not meeting the food group distribution prescribed in dietary guidance. A pattern name such as “low fruit and vegetable” or “unbalanced” might be less misleading.

**Recommendations for only WGFs may impair nutrient status and lower WG consumption**

RGFs, especially enriched or fortified staples, provide nutrients which are potentially at risk if RGF consumption is limited. REGs have reduced the percentage of the US population failing to meet the estimated average requirement as follows: iron, from 22% of the population to 7%; thiamin, from 51% to 4%; vitamin B-6, from 22% to 12%; riboflavin, from 11% to 1.7%; and folate, from 88% to 11% (134).

Near-daily RTEC (WG or RG) consumption was associated with increased milk, yogurt, and fruit consumption and lower risks of inadequate intakes of vitamin A, calcium, folate, vitamin B-6, magnesium, and zinc (136–138, 168).

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**Table 1** Percentages by food category of weekly servings of foods classed as WGs and RGs in most epidemiological studies.

| WG food categories | Percentage of weekly servings | Recommended staple (core) food |
|--------------------|-------------------------------|--------------------------------|
| Dark bread         | 60.5                          | Yes                            |
| WG ready-to-eat    | 17.6                          | Yes                            |
| Cereal             |                               |                                 |
| Popcorn            | 13.4                          | At times³                       |
| Oatmeal            | 6.8                           | Yes                            |
| Wheat germ         | 1.5                           | Yes                            |
| Brown rice/rice mixes | 1.3                        | Yes                            |
| Bran               | 0.6                           | Yes                            |
| Other⁴            | 0.3                           | Yes                            |
| RG food categories |                               |                                 |
| White bread and pita | 29.9                      | Yes                            |
| Pasta              | 5.0                           | Yes                            |
| English muffins,  | 4.7                           | Yes                            |
| Bagels, rolls      |                               |                                 |
| RG breakfast cereal | 3.9                         | Yes                            |
| White rice and mixes | 3.4                       | Yes                            |
| Pizza crust        | 2.5                           | At times                        |
| Sweets/desserts    | 45.2                          | No                             |
| Muffins or biscuits | 3.2                         | At times                        |
| Sweet rolls        | 2.6                           | No                             |
| Pancakes or waffles | 22.6                        | At times                        |
| Crackers⁵         | Not included in initial study | At times                        |

¹RG, refined grain; WG, whole grain.
²Percentages of weekly WG servings for WG foods; percentages of weekly RG servings for RG foods. Data are from the Iowa Women’s Health Study (31, 32). Proportions of intakes from indulgent grains, RGs, and staple ones were similar in subsequent studies, such as references 33–37.
³An “at times” designation suggests the food in question could be a recommended staple if prepared with little sugar or saturated or total fat.
⁴Bulgur, kasha, couscous, barley
⁵All crackers were deemed as RG regardless of their WG content.
Despite contributing to higher sugars, both RG and WG RTECs were associated, in a systematic review of 64 studies, with dietary patterns containing more DF and micronutrients (135). Nutrient availability may be enhanced from REGs because of specific fortificants used and fewer bran components that impair absorption (136, 137, 168, 170).

Mandatory (and voluntary) folate fortification of RG flour in many jurisdictions deserve mention as an initiative that is helping to decrease the incidence of spina bifida, anencephaly, and other birth defects (171, 172). The importance of REGs or fortified grains is demonstrated in a study of US women. In the year before conception, women adhering to dietary regimens avoiding grains or carbohydrates were associated with having a 30% increase in risk of folate-related birth defects in their offspring (172,173).

DF also deserves a mention, because only 4% of the US population ingests the recommended amount of DF (174–177). Although WGFs contribute 15.3% of the total US DF, and would contribute more if more were eaten, recommendations for exclusive WGF intake fail to consider that RGFs provide 54.5% of the DF consumed (175–177).

GBFs are the only source of cereal fiber, and various fibers are needed to meet all the fibers’ functions (178). Because DF is “a nutrient of concern,” research is needed to show that recommendations for no GBFs or no RGFs lower neither total DF nor cereal fiber intakes.

Recommendations for ingestion of only WGFs extrapolate beyond existing data

In the highest quintiles of most cohorts, median WGF consumption is ~3 servings/d (~80–90 g WGF/d or 48 g WG/d). Although regions such as Scandinavia have higher WGF consumption, the foods include WG rye, barley, and oats (67). Thus, extrapolating from these data to other populations may not be predictive. Further, intervention data (52–61, 71, 95–101), even where all WGFs were substituted for RGFs, yield inconsistent results.

In the US NHANES (2009–2012; 2012–2014) and the Canadian Community Health Survey (2015), the right mix of WGFs and RGFs is supported by cross-sectional and epidemiological data from both children and adults (176, 177, 179–180) and is associated with better nutrient and body weight measures than intake of all WGFs or no grains (135). Data from the Framingham Heart cohort showed the lowest VAT was associated with the ingestion of 3 WGF and 2 RGF servings (35). Because WGFs may contain 49–74% RGs, positive health outcomes associated with WGFs tacitly argue for the mix of WGs and RGs recommended in dietary guidance.

Dietary pattern research supports the right mix of RGs and WGs

Vetted, balanced patterns [e.g., MyPlate, Dietary Approaches to Stop Hypertension (DASH), or MEDiet] demonstrate the health impact of diets with 50% carbohydrate and the right mix of foods including GBFs (5, 6, 10, 181–184). Analyses of the DASH diet or MEDiet (182–184) show a mix of 35% RGs and 23% WGFs. Thus, cross-sectional, epidemiological, and dietary pattern research suggests associations with positive health outcomes when total grain consumption meets recommendations and is comprised of roughly half RGs and WGs.

Conclusions

A dietary balance of GBFs and carbohydrates is associated with better nutrient intake and health measures. A recent meta-analysis showed that the lowest all-cause mortality risk was associated with 50% of E coming from carbohydrate (185). Epidemiological findings consistently show that ingestion of three 30-g WGF servings/d (48 g WGs/d) is associated with reduced chronic disease risk. However, findings from RCTs that replace all RGFs with WGFs yield inconsistent results. Many of the same studies that show WGFs are associated with better health outcomes also show that RGFs, especially staples, eaten in recommended amounts, are not independently associated with increased risk. Very high intakes of specific RGFs such as rice are associated with increased risks in certain populations. However, the variability and potential residual confounding among studies make attribution of risks to rice or RGFs problematic.

Outcomes of epidemiological studies skew toward WGs for the following reasons. 1) Multiple confounding occurs because WG eaters have healthy behaviors (and vice versa), thus amplifying the health benefits of WGF consumption. 2) Varying WGF definitions make comparison of study outcomes challenging and mean that WGFs may contain between 49% and 74% RGs, which argues for a mix of WGs and RGs. 3) Binary categorization of GBFs creates inadvertent bias in favor of WGFs because the WGF categories are comprised almost exclusively of recommended GBFs, whereas the RG category consists of half recommended and half indulgent GBFs. Reanalysis of food intake data separating indulgent GBFs from staple ones could be useful. 4) GBF intake is unbalanced. Some consumers overconsume GBFs, mostly as RGFs and often indulgent RGFs. Nearly all populations underconsume WGFs (186–194). This imbalance coupled with overconsumption of RGFs amplifies negative impacts of RGFs. 5) Food pattern names such as “white bread” may subtly direct thoughts to the named food (e.g., white bread), not to the dietary imbalance or foods missing from the pattern.

Some advocate that all GBFs should be WGFs, despite evidence showing that RGFs, especially staples eaten in recommended amounts, are not independently associated with increased risk. Nevertheless, some health professionals and groups such as the 2019 EAT–Lancet Commission deem RGFs as “unhealthful plant-based foods,” categorize them with other dietary pariahs—processed meats, sweets, and SSBs—and suggest their reduction or elimination (195–198).

Recommendations that GBFs should be all WGFs extrapolate beyond the existing data. In most cohorts the quintile eating the most WGFs ingests ~3 servings/d or 90 g/d (~48 g/d WG). Extrapolation using data from populations with higher consumption may not be applicable to cohorts.
where lifestyle, diet, and mix of WGFs (wheat, rye, barley, and oats) differ.

Important nutritional contributions of RGs, especially REGs, to iron, folate, and B-vitamin intakes may be disregarded by those zealously recommending all WGFs. Further, findings from vetted patterns, such as the MEDiet where the mix of WGFs and RGs contributes to healthy outcomes, may be overlooked. RGs can make WGFs more acceptable and, thereby, improve WG intake. Inclusion of GBFs can aid long-term dietary compliance and create sustainable dietary change by contributing plant-based protein, dietary fiber, and nutrients in forms that are acceptable, familiar, affordable, and shelf-stable. Recommendations for GBFs need to be crafted so that consumers aim to ingest the recommended number of servings of GBFs (mostly staples) to meet E needs, and so that consumers replace half the RGF servings with WGFs. These points affirm the role of GBFs in the diet and support recommendations that consumers “make at least half their grains whole.”

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