Carbohydrate Quality: What Do I Tell My Patients?

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Introduction Obesity and diabetes have reached epidemic proportions and are projected to increase over the next decade with important consequences for their downstream cardiometabolic complications. As the role of fat in this dual epidemic has been placed in doubt, carbohydrates are increasingly being indicted as the main culprit. Much of the concern has focused on the absolute amount and proportion of carbohydrates in the diet with all sources including traditional carbohydrate staples like cereal grains, pulses, and pasta coming under attack in the mainstream media, popular books, social media, the medical literature, and statements of prominent advocacy groups.

The "carbohydrate-insulin model" has been proposed to explain the ability of carbohydrate to contribute to obesity and its downstream cardiometabolic complications. This model posits that an overabundance of carbohydrate leads to endocrine dysregulation marked by hyperinsulinemia, which drives fuel partitioning with carbohydrate directed away from metabolically active tissue (eg, skeletal muscle, heart, lung, liver, etc.) to adipose tissue, resulting in a state of "cellular internal starvation" with compensatory increases in dietary intake and decreases in energy expenditure leading to weight gain. Although the model has confirmed that low carbohydrate diets produce the requisite decrease in insulin, these diets have failed to achieve the predicted weight loss benefit. A series of very carefully controlled, randomized, inpatient feeding trials at the National Institutes of Health (NIH), were unable to achieve the predicted increases in energy expenditure and body fat loss comparing low carbohydrate diets with high carbohydrate diets.[1,2] While it can be argued that the ability of low carbohydrate diets to induce decreases in energy intake through alterations in food intake regulation or to stimulate spontaneous increases in physical activity were not assessed (as both variables were tightly clamped), a large database of long-term randomized controlled trials conducted under free-living conditions (in which these mechanisms could manifest) have not shown any advantages of low carbohydrate diets over high carbohydrate diets. A network meta-analysis of 48 unique randomized trials involving 7,286 participants of diets of varying macronutrient profiles, and subsequent randomized trials, have not shown differences in weight loss at 6-months and 12-months of follow-up. Irrespective of the carbohydrate content, the most important determinant of success in these trials has been adherence to any one diet or macronutrient distribution, and clinic attendance.[3]

Although the evidence from randomized trials has failed to show the predicted advantages of low carbohydrate diets for weight loss and the downstream cardiometabolic improvements, large prospective cohort studies suggest that high carbohydrate diets may still have an adverse association with important cardiometabolic disease outcomes. An analysis of the Prospective Urban and Rural Epidemiological (PURE) cohort study in 135,335 participants free of cardiovascular disease from 18 low-income, middle-income, and high-income countries showed increased cardiovascular and all-cause mortality comparing the highest with the lowest quantiles of carbohydrate exposure, independent of the type of carbohydrate over 10 years of follow-up. Another simultaneously published analysis of the PURE study, however, suggested that the type of carbohydrate may modify the association with carbohydrate sources from legumes and fruit showing the opposite association: a cardiovascular mortality and all-cause mortality benefit.[4]

A more important focus may be on carbohydrate quality rather than quantity for cardiometabolic health. Carbohydrate quality can be defined broadly across 4 main domains: low glycemic index/load (GI/GL), high fiber, food-based approaches emphasizing specific carbohydrate-containing foods (whole grains, pulses, and fruit), and low sugars (Fig 1). A careful review of the best available evidence from prospective cohort studies of clinical outcomes and

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randomized controlled trials of intermediate endpoints follows for each domain of carbohydrate quality.

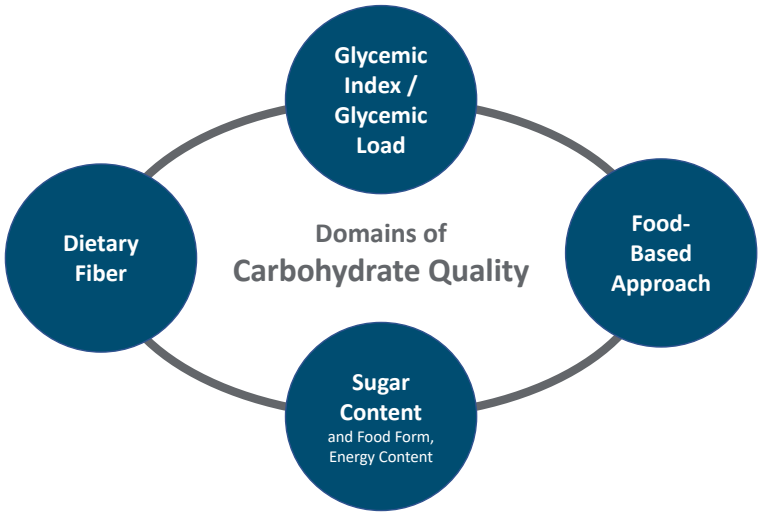

Fig 1. Four domains of carbohydrate quality.
Food-based approach includes whole grains, pulses (beans, peas, chickpeas, and lentils), and fruit.

Glycemic Index/Load (GI/GL) Low GI or GL dietary patterns have shown evidence of advantages for the prevention and management of cardiometabolic diseases in the context of moderate to high carbohydrate intakes. Systematic reviews and meta-analyses of >20 prospective cohort studies in >600,000 participants have shown that low GI and GL dietary patterns are associated with decreases in diabetes and cardiovascular disease incidence compared with high GI and GL dietary patterns up to 25 years of follow-up.[5] This line of evidence agrees with the available evidence from randomized controlled trials of the effect of GI and GL on intermediate cardiometabolic risk factors. Systematic reviews and meta-analyses of >50 randomized controlled trials in >4000 participants show that low GI and GL dietary patterns lead to weight loss/maintenance, and a clinically meaningful improvement in glycemic control by HbA1c of ~0.5% (a level that is at the lower limit of efficacy of most antihyperglycemic agents, and exceeds the minimally meaningful threshold for new drug development set by the FDA), as well as improvements in blood lipids, and blood pressure compared with higher GI and GL dietary patterns.[5]

Dietary Fiber High fiber dietary patterns have shown evidence of advantages for the prevention and management of cardiometabolic diseases in the context of high carbohydrate intakes. Systematic reviews and meta-analyses of ≥10 prospective cohort studies in >1,000,000 participants have shown that total fiber, independent of source (cereals, vegetables, or fruit) or type (insoluble versus soluble), is associated with decreased incidence of diabetes and cardiovascular disease when comparing the highest with the lowest levels of fiber intake up to 19 years of follow-up.[6] The evidence from randomized controlled trials, however, suggests that improvements in intermediate cardiometabolic risk factors is most reliably linked to sources of viscous soluble fiber. Systematic reviews and meta-analyses of >100 randomized controlled trials in >5,000 participants show that high viscous soluble fiber intake from oats, barley, psyllium, and konjac mannan result in improvements in blood lipids (for which there are approved health claims in Canada, US, and Europe), glycemic control, and blood pressure.[7]

Food-Based Approaches Dietary patterns emphasizing specific carbohydrate-containing foods that include whole grains, dietary pulses (beans, peas, chickpeas, and lentils), and fruit have shown evidence of advantages for the prevention and management of cardiometabolic diseases in the context of high carbohydrate intakes. Systematic reviews and meta-analyses of prospective cohort studies have shown that high intakes of whole grains (>15 studies in >400,000 participants with follow-up to 25 years), dietary pulses (8 studies in >200,000 participants with follow-up to 29 years), and fruit (>10 studies in >500,000 participants with follow-up to 23 years) are associated with decreases in cardiovascular disease and diabetes incidence, and cardiovascular and all-cause mortality in the case of whole grains and fruit.[8-10] This line of evidence is generally concordant with evidence from randomized controlled trials of the effect of whole grains, dietary pulses, and fruit on intermediate cardiometabolic risk factors. Systematic reviews and meta-

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analyses of randomized controlled trials show that dietary patterns emphasizing dietary pulses (>50 trials in >1,000 participants with follow-up to 1 year) or fruit (>20 trials in >1,000 participants with follow-up to 6 months) result in weight loss/maintenance; and improved glycemic control, blood lipids, and blood pressure.[9,11] The systematic reviews and meta-analyses of whole grains (>25 trials in >2,000 participants with follow-up to 16 weeks), however, suggest that the improvements are restricted to whole grain sources from oats and barley.[12]

Sugars Any benefit of low sugar dietary patterns appears to be dependent on food form and energy control. Most of the evidence supporting public health recommendations to limit sugars derives from sugar-sweetened beverages (SSBs). Although systematic reviews and meta-analyses of >15 prospective cohort studies in >400,000 participants have shown an adverse association of SSBs with incidence of obesity, diabetes, heart disease, and stroke, these adverse associations are markedly attenuated with adjustment for energy (hence, many investigators do not adjust for energy as it is considered to be on the causal pathway between the exposure [sugars] and the outcome [cardiometabolic diseases]), and do not hold when modeling the total, added or free sugars they contain independent of food form.[13] Other important food sources of sugars from grains and grain products, dairy and dairy products, and fruit and fruit products have also failed to show harmful associations, and have even shown protective associations in the case of fruit, 100% fruit juice, yogurt, and breakfast cereals.[13] These conditional associations are supported by the evidence from randomized controlled trials of fructose, the sugar moiety to which harm has been attributed, owing to its unique set of metabolic and endocrine responses. Systematic reviews and meta-analyses of >50 randomized controlled trials in >1,000 participants have shown that fructose, in energy matched substitutions with other carbohydrates (mainly starch), does not show adverse effects on intermediate cardiometabolic risk factors, and even shows advantages for glycemic control and blood pressure. Adverse effects are only seen when fructose supplemented diets with excess energy compared to the same diets without the excess energy, suggesting that any harm relates to the excess energy rather than any special mechanisms attributed to fructose-containing sugars.[13]

Unintended Consequences of a Focus on Carbohydrate Quantity A singular focus on carbohydrate quantity over quality may have important unintended consequences. One concern is that we may get a repeat of the "low fat" paradigm, in which manufacturers produce "low carbohydrate" foods that, like their "low fat" predecessors, are of no or less nutritional value and similar caloric content. If the consumer believes that they are "healthier", then the response may be overconsumption with no benefit or even harm to public health. Another concern is that a focus on "low carbohydrate" foods may take attention away from more important dietary risk factors. The Global Burden of Disease Project, a massive pooling project that allows for a comparative analysis of the global burden of disease attributable to the leading 79 risk factors using population attributable risk fraction modeling, provides important evidence that making carbohydrate quantity a public health priority would be misleading.[14] The most recent update does not identify high carbohydrate intake from foods (with the exception of SSBs) as a dietary risk factor. On the contrary, low intakes of various domains of carbohydrate quality are identified as dietary risk factors that increase premature morbidity and mortality, with low intakes of whole grains (1st), fruit (2nd), and fiber (6th) explaining ~1/3 of the burden of disease attributable to 14 dietary risk factors in North America. Some maneuvers used to achieve low carbohydrate diets, such as high intake of processed meat or red meat, are also identified as dietary risk factors that increase premature morbidity and mortality.

The Path Forward: What Do I Tell My Patients? Dietary guidelines are already moving away from a focus on single nutrients, such as carbohydrates, to more food and dietary pattern based recommendations. This shift recognizes that a focus on single nutrients misses important interactions between different nutrients, the nutrients and the food form/matrix, and the foods and the dietary patterns in which they are contained. There is also recognition that no one diet "fits all", and adherence is one of the most important determinants of the success of any

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dietary approach. One must consider that there are a number of dietary patterns with evidence of advantages and disadvantages, and this evidence must be aligned with the values, preferences and treatment goals of the individual to achieve the greatest adherence over the long term.[15]

Conclusions Carbohydrate quality appears to be a more important consideration than carbohydrate quantity. Although some people may benefit from a low carbohydrate dietary pattern, others may benefit from high carbohydrate dietary patterns that are low in GI, high in fiber (especially viscous fiber sources), or emphasize specific foods such as whole grains (especially oat or barley sources), pulses, or fruit. The best evidence from systematic reviews and meta-analyses of the available evidence shows that these domains of carbohydrate quality are associated with decreased weight gain, diabetes incidence, and cardiovascular disease incidence and mortality in prospective cohort studies, and decrease intermediate cardiometabolic risk factors in randomized controlled trials. The evidence for sugars as a domain of carbohydrate quality appears to be highly dependent on food form and energy. These data reflect the current shift in dietary guidance away from reductionist "one-size-fits-all" nutrient-centric recommendations (eg, "low fat", "low carb"), to food and dietary pattern-based recommendations that allow for flexibility in the proportion of carbohydrates in the diet, with a focus on quality over quantity and dietary patterns over single nutrients.

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