Dietary carbohydrates: role of quality and quantity in chronic disease

David S Ludwig and colleagues examine the links between different types of carbohydrate and health

Carbohydrate is the only macronutrient with no established minimum requirement. Although many populations have thrived with carbohydrate as their main source of energy, others have done so with few if any carbohydrate containing foods throughout much of the year (eg, traditional diets of the Inuit, Laplanders, and some Native Americans).[1 2] If carbohydrate is not necessary for survival, it raises questions about the amount and type of this macronutrient needed for optimal health, longevity, and sustainability. This review focuses on these current controversies, with special focus on obesity, diabetes, cardiovascular disease, cancer, and early death.

Role of carbohydrate consumption in human development

The large brain of modern humans is energetically expensive, requiring a disproportionate share of dietary energy compared with that of other primates. The first hunting and gathering societies were characterised by greater consumption of not only animal foods but also plant foods with greater carbohydrate availability than leaves—including ripe fruit, honey, and eventually cooked starchy foods.[3 4] The higher nutrient and energy density of this diet allowed for evolution of a smaller gastrointestinal tract, offsetting the energy demands of the brain.[5]

KEY MESSAGES

- Human populations have thrived on diets with widely varying carbohydrate content
- Carbohydrate quality has a major influence on risk for numerous chronic diseases
- Replacing processed carbohydrates with unprocessed carbohydrates or healthy fats would greatly benefit public health
- The benefit of replacing fructose containing sugars with other processed carbohydrates is unclear
- People with severe insulin resistance or diabetes may benefit from reduction of total carbohydrate intake

As a result of selective pressures related to dietary changes, two major gene adaptations occurred affecting carbohydrate digestion: average salivary amylase gene copy number (AMY1) increased more than threefold, with substantial variation among populations related to starch consumption[6]; and lactase persistence into adulthood developed in multiple geographically distinct populations, facilitating digestion of the milk sugar lactose.[7] After our transition to an agrarian lifestyle in the Neolithic period, beginning 12 000 to 14 000 years ago, total carbohydrate intake increased substantially as grains became a dietary staple, but archaeological evidence shows that diet related problems also emerged, including endemic nutrient deficiencies, a decrease in mean height, and dental caries.[8-10]

Relation between carbohydrate types and health outcomes

Carbohydrates are formally defined as containing carbon, hydrogen, and oxygen in the ratio of 1:2:1. In practice, dietary carbohydrates comprise compounds that can be digested or metabolically transformed directly into glucose, or that undergo oxidation into pyruvate, including some sugar alcohols (eg, sorbitol). Several systems for classifying carbohydrates have been in use, with varying relevance to health outcomes.

Chain length

Carbohydrates can be categorised according to degree of polymerisation into monosaccharides (monomers), disaccharides, oligosaccharides, and polysaccharides (starch). Conventionally, carbohydrate polymer length is believed to determine the rate of digestion and absorption, and therefore the rise in blood glucose after eating. People with diabetes were therefore instructed to avoid sugars and emphasise starchy foods.[11] However, research beginning 50 years ago showed no meaningful relation between carbohydrate chain length and postprandial glycaemia or insulinaemia.[12 13] Modern starchy foods such as bread, potatoes, and rice raise blood glucose and insulin substantially more than some high sugar foods (eg, whole fruits).[14] By contrast, some traditionally consumed starches (legumes, whole kernel grains, pasta, long fermentation sourdough bread) release glucose more slowly because the starch is protected from digestion by the food matrix (gelatinised) or because the presence of organic acids slows gastric emptying.

Glycaemic index and glycaemic load

Although carbohydrates are the only food constituents that directly increase blood glucose (the main determinant of insulin secretion), population studies suggest that the total amount of carbohydrate as a percentage of dietary energy is less important than the carbohydrate type for risk of chronic disease. Refined grains, potatoes, and sugar sweetened beverages are associated with increased risk,[15] whereas minimally processed grains, legumes, and whole fruits are associated with reduced risk.[16] This distinction may be explained partly by differences in how specific carbohydrates affect postprandial hyperglycaemia and hyperinsulinaema, which are causally related to the development of type 2 diabetes, coronary heart disease, and perhaps obesity.[17]

Two empirical metrics have been introduced to rank foods according to effects on blood glucose: glycaemic index (GI) and glycaemic load (GL) (table 1). The GI compares foods based on a standardised amount of available carbohydrate. Glycaemic load (GI multiplied by the amount of carbohydrate in a typical serving) allows the glycaemic effect of foods, meals, and whole diets to be compared as realistically consumed, and it has been shown to be a better predictor of glycaemic response than the amounts of carbohydrate, protein, and fat in food.[18] Prospective observational studies have reported that higher energy adjusted GI or total GL is an independent risk factor for type 2 diabetes in men and women[19]; cardiovascular morbidity and mortality, including stroke, in women[20-22]; and certain types of cancers in both sexes,[23 24] though some have questioned the strength and consistency of these findings.[25]

Fibre and resistant starch

Fibre or non-starch polysaccharide is plant carbohydrate that is not digestible by human enzymes. Fibre and resistant starch provide, to varying degrees, substrate for

Table 1 | Carbohydrate content and glycaemic index of representative foods

Food	Serving size (g)	Available carbohydrate* (g) per serving	Glycaemic index†	Glycaemic load
Rice, jasmine, boiled	120	32	86	28
Instant oat porridge/oatmeal	250	26	79	21
Rice, basmati, boiled	120	30	57	17
Potato, boiled	150	20	78	16
Breakfast cereal, flaked	30	22	72	16
Pasta, white or brown, boiled	120	31	49	15
Bread, white or brown	40	19	75	14
Traditional oat porridge	250	24	55	13
Fruit juice	250 mL	24	50	12
Fruit, tropical	120	16	58	9
Barley, boiled	120	34	28	9
Bread, wholemeal	40	13	54	7
Legumes, boiled	150	22	31	7
Fruit, temperate	120	14	42	6
Pumpkin, boiled	75	8	64	5
Milk	250 mL	12	32	4
Nuts	30	7	25	2

*Available carbohydrate may vary depending on specific brand or country of origin
†GI data are average values adapted from Atkinson et al[14] and unpublished observations from the Sydney University Glycemic Index Research Service, 2018.

colonic microbial fermentation, leading to the production of short chain fatty acids that provide a direct energy source for colonic epithelium and influence hepatic insulin sensitivity.[26] Fibre can be classed as soluble (viscous or non-viscous) and non-soluble, properties that influence gastrointestinal absorption and metabolic effects. Viscous fibres such as vegetable gums and those derived from fruits, legumes, and psyllium slow down digestion and reduce postprandial glycaemia and cholesterol absorption, whereas insoluble fibres (eg, from wheat bran) have limited metabolic actions.

Added and free sugar

Added sugars are defined as sugars that are added to foods during food processing, manufacturing, or preparation. The newer term, "free sugars," also includes sugars naturally present in unsweetened fruit juices: otherwise, these two terms are interchangeable. Under this definition, only lactose naturally present in milk products and sugars contained within the cellular structure of foods (eg, whole fruits) would be excluded.[27]

Most health authorities agree that overconsumption of added sugars, and particularly sugar sweetened drinks, has contributed to the obesity epidemic.[27] In the higher quality prospective observational studies, changes in consumption of sugary drinks are directly associated with changes in energy intake[28] and body weight.[29] Furthermore, two large randomised controlled trials found that elimination of sugary drinks reduced body weight among adolescents at one year[30] and among younger children at 18 months.[31] In meta-analyses of trials in adults consuming unrestricted diets, reduced intake of added sugars is associated with a modest decrease in body weight, while higher intake is associated with a comparable gain. Isocaloric substitution of sugars for other carbohydrate, however, did not affect body weight.[32]

The potential mechanisms relating sugar to weight gain remain a topic of debate. Several investigators have highlighted the potential role of fructose.[33-39] Fructose is metabolised primarily in the gut and liver and, under certain experimental conditions, can stimulate de novo lipogenesis, inflammation, and insulin resistance. However, the relevance of these findings to typical consumption patterns has been questioned.[40 41] Moreover, high intakes of fruits with relatively high amounts of fructose are associated with good metabolic health, suggesting that the food source of fructose is also important.[42]

The relative contribution of added sugar versus other carbohydrates to the obesity epidemic remains unknown. Indeed, high GL starchy foods (without fructose) contribute substantially more calories to typical Western diets than added sugar.[43] In Australia, intakes of added sugars and sugar sweetened drinks have progressively declined since the 1990s, even as mean body mass index in adults and children has risen sharply.[44]

Beyond body weight, meta-analyses of randomised trials indicate that higher intakes of added sugars raise triglycerides, total cholesterol, blood pressure, and other risk factors for cardiovascular disease.[38 45-47] Of special concern is non-alcoholic fatty liver disease, an obesity related condition that has emerged as a major public health threat. Reduction of fructose or sugar consumption in several clinical trials resulted in lower intrahepatic fat.[48-50] However, each of these studies has design limitations, such as lack of a control group and confounding by unintended weight loss. In a six month trial, people consuming sugar sweetened drinks had higher levels of liver and ectopic fat than those consuming drinks without added sugar, even though body weight did not differ by diet group.[47]

Based on the finding that "increasing or decreasing free sugars is associated with parallel changes in body weight … regardless of the level of intake of free sugars," the 2015 WHO guidelines recommended that consumption of free sugars should be less than 10% of energy intake for both adults and children, with potential additional benefits below 5%.[27] The Scientific Advisory Committee on Nutrition in the UK recommended a 5% upper limit, noting potential benefits at this lower level for dental health and total energy intake.[51] (Modern starchy foods may also contribute to dental carries.[52]) The *2015-2020 Dietary Guidelines for Americans* recommend a limit on added sugars of 10% total energy.[53]

Composite quality indices

Beyond the mechanisms implied by these broad classification systems, carbohydrate containing foods may influence health in various other ways. Whole plant foods contain myriad compounds with demonstrably beneficial (vitamins, minerals, and antioxidant and anti-inflammatory phytochemicals) or possibly adverse [54] (lectins, phytates) actions. Ultimately, diet must be considered in an integrated fashion, with changes in consumption of one category of food affecting others. The nature of these exchanges will determine the apparent healthfulness of specific foods in population studies. Recognising this challenge, several indices for carbohydrate quality (based on GI, fibre, whole:total grain consumption, and other factors) and total diet quality have been proposed.

How do carbohydrate containing foods affect health?

Grains

Grains—the seeds of cereal grasses and similar plant families—are staple foods and a major source of dietary carbohydrate worldwide. Minimally processed whole grains retain all three components of the seed. Refined grains are processed to remove the protein and fat rich germ and fibre rich bran, leaving only the starchy endosperm. Meta-analyses of randomised clinical trials indicate that, compared with diets without them, whole grains produce small but significant reductions in low density lipoprotein (LDL) cholesterol, total

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cholesterol, and percentage body fat; they also improve postprandial glucose levels and glucose homeostasis.[55-57]

Prospective cohort studies have also shown significant inverse associations between whole grain intake and incidence of type 2 diabetes, coronary heart disease, ischaemic stroke, total cardiovascular disease, and several cancers, as well as risk of death from all causes.[58-62] Conversely, greater refined grain intake, especially from white rice, is associated with an increased risk of type 2 diabetes.[59 63] Whole kernel or coarsely milled grains tend to have lower GI than refined grains and contain higher amounts of fibre and phytochemicals with potential anti-inflammatory and antioxidant properties.

However, the relative health benefits of whole grains and wholemeal foods compared with other categories of whole foods with lower carbohydrate content (eg, nuts, seeds, legumes, avocado, olives) has not been well studied. Furthermore, most whole grains in processed foods do not contain the intact whole grain kernel but have been milled into a fine particle size (thus higher GI) flour, with varying amounts of bran and germ reincorporated. Therefore, food labelled as whole grain may not have the same health benefits as intact or minimally processed whole kernel grains (wheat berries, steel cut oats, quinoa), and some whole grain foods contain high amounts of added sugar.

Potatoes

Potatoes, the leading vegetable food in most countries, are another major source of dietary carbohydrate. Although potatoes have some nutrients (such as vitamin C, potassium, and fibre), they contain predominantly starch with a high GI as typically eaten.[14] In three cohorts of US men and women, increased intake of potatoes was associated with greater weight gain[64] and higher risk of type 2 diabetes, even after adjustment for body mass index and other diabetes risk factors.[65] In the same cohorts, higher intake of baked, boiled, or mashed potatoes and French fries was independently associated with an increased risk of developing hypertension.[66] Thus, the health effects of potatoes more closely resemble those of refined grains than those of other vegetables.

Legumes

Legumes such as beans, peas, and lentils, like whole grains, improve nutritional quality and health outcomes when included in typical dietary patterns. Legumes contain low GI carbohydrate and relatively high amounts of protein, fibre, and other nutrients.[14 67] A meta-analysis of randomised clinical trials found a significant decrease in total and LDL cholesterol for non-soy legume dietary interventions compared with control diets.[68] Another meta-analysis found a 10% lower risk of cardiovascular disease comparing the highest with the lowest categories of consumption.[69] In a Costa Rican population, increasing the ratio of beans to white rice was associated with lower cardiometabolic risk factors, including blood lipids and blood pressure.[70]

Fruits

Whole fruits are high in fibre, vitamins, minerals, and phytochemicals and typically have moderate to low GL.[14] Regular consumption of fruits is associated with lower risk of type 2 diabetes, cardiovascular disease, cancer, and all-cause mortality in prospective cohort studies.[71-73] Greater consumption of whole fruits (especially blueberries, grapes, and apples) is significantly associated with lower risk of diabetes, whereas greater consumption of fruit juices is associated with a higher risk in three US cohorts.[74] Compared with whole fruits, fruit juices tend to have less fibre, fewer micronutrients, and higher GI,[75] and for these reasons, classifying whole fruits and juices together in dietary recommendations is controversial.

What are the metabolic effects of carbohydrates in populations?

Residents in places associated with extreme longevity have traditionally consumed high carbohydrate diets, although associated healthy lifestyle factors may confound a causal interpretation.[76] By contrast, the PURE study in 18 countries reported that higher carbohydrate intake was associated with increased mortality, but here too, confounding is possible (eg, many people in low income countries subsist predominantly on starchy foods such as white rice).[77 78] In long term large cohorts studied in the US, total carbohydrate intake is also associated with higher mortality, though the type of dietary fat importantly modified risk.[79] Analogously, substitution of saturated fat with low GI carbohydrate is associated with lower risk of myocardial infarction, whereas substitution with high GI carbohydrates is associated with higher risk.[80]

Clinical trials have shown that low carbohydrate diets produce greater weight loss than lower fat diets in the short term, but this difference diminishes with time because of poor long term compliance.[81-85] The recent DIETFITs study reported a non-significant advantage for a healthy low carbohydrate versus healthy low fat diet, but both groups were counselled to limit sugar, refined grains, and processed foods in general.[86] Thus evidence suggests that the type of carbohydrates may have a greater effect on health outcomes than total amount for the general population. However, specific groups may respond differently to the carbohydrate quantity and quality.

Insulin resistance, metabolic syndrome, and diabetes

The metabolic syndrome (characterised by central adiposity, hypertension, dyslipidaemia, hyperglycaemia, and chronic inflammation) contributes importantly to risk of diabetes and cardiovascular disease worldwide. An underlying cause of this syndrome is insulin resistance and the associated increase in circulating insulin levels. Since insulin resistance reflects diminished ability to promote uptake of glucose into target organs, some investigators have proposed a reduced carbohydrate diet as part of treatment.[87] Observational and experimental data suggest that people with low levels of physical activity or obesity (major contributors to insulin resistance) may be especially sensitive to the adverse metabolic effects of diets high in sugar or GL[88 89]—perhaps explaining how Asian farming societies can maintain low adiposity and cardiovascular disease rates on white rice based diets.

People with diabetes may particularly benefit from reducing consumption of foods that increase postprandial blood glucose. Preliminary evidence suggests improved glycaemic control, lower triglycerides, and other metabolic advantages from low carbohydrate or low GI diets in both type 1[90] and type 2 diabetes,[91] though long term data on efficacy and safety are lacking.

Early insulin secretion

Early insulin secretion reflects the tendency of the pancreatic □ cells to release insulin rapidly after carbohydrate ingestion. This clinical measure, distinct from insulin resistance, can be assessed as the blood insulin concentration 30 minutes into a standard oral glucose tolerance test (insulin 30).[92] According to the carbohydrate-insulin model of obesity, people with high insulin secretion would be especially susceptible to weight gain on a high GL diet, a hypothesis with some support from laboratory, observational, and clinical research.[93-95] High insulin action in adipose tissue may have an anabolic effect that promotes fat deposition, leading to increased hunger and lower energy expenditure. A recent Mendelian randomisation study found that genetically determined insulin 30 results strongly predicted body mass index.[96] However, neither insulin 30 nor genetic risk was found to modify response to diet in DIETFITS, although GL was notably low in both diet groups of that study.[86]

Box 1: Carbohydrate controversies

- Would reduction in total carbohydrate intake (currently typically 45-65% of total energy) help control body weight in general population and susceptible subgroups?
- What is the role of a low carbohydrate diet in prevention and treatment of metabolic syndrome and type 2 diabetes, and in management of type 1 diabetes?
- Does ketosis induced by severe carbohydrate restriction provide any unique metabolic benefits and, if so, in what clinical settings would this diet be advisable?
- To what level should added (or free) sugars be restricted for optimum individual health and for the population as a whole?
- Would substitution of fructose in added sugars with glucose based sweeteners provide metabolic benefit or harm?
- Would substitution of free sugars with poorly digestible sugars, sugar alcohols, or artificial sweeteners provide health benefits or harms (eg, unexpected effects on the microbiome)?
- Would increased intake of resistant starch provide health benefits?
- What are the health effects of substituting whole grains with other high carbohydrate (fruits, legumes) or high fat (nuts, seeds, avocado) whole plant foods?
- What are the long term effects of different types of carbohydrates on population risk of cancer, neurodegenerative diseases, and cognitive function?
- Which carbohydrate based foods will provide an optimal combination of health benefits, environmental sustainability, cost, and public acceptability?

Salivary amylase

The diploid copy number of the salivary amylase gene (AMY1) varies widely, affecting amylase protein concentration in saliva. People with higher copy numbers have higher postprandial glycaemia after consumption of starchy (but not sugary) foods.[97] High AMY1 copy number may have provided a survival advantage, but its relevance to obesity and metabolic disease today remains unclear.[98-100] A recent study reported a diet-gene interaction such that the lowest body mass index was observed among people with high starch intake and low AMY1 copy number (reflecting low genetic capacity to digest starch).[99]

Conclusions

Although human populations have thrived on diets with widely varying macronutrient ratios, the recent influx of rapidly digestible, high GI carbohydrates in developed nations has contributed to the epidemics of obesity and cardiometabolic disease. Moreover, the traditional starch based diets of some developing nations have likely contributed to rising risk of chronic disease, with the decrease in physical activity and higher body mass index associated with rapid urbanisation.

However, carbohydrate quality seems to have a more important role in population health than carbohydrate amount. A strong case can be made for consumption of high GL grains, potato products, and added sugars (especially in drinks) being causally related to obesity, diabetes, cardiovascular disease, and some cancers; whereas non-starchy vegetables, whole fruits, legumes, and whole kernel grains appear protective. Nevertheless, the metabolic effects of total and high GI carbohydrate may vary among individuals, depending on the degree of insulin resistance, glucose intolerance, or other inherited or acquired biological predispositions.

Despite much new knowledge about the metabolic effects of carbohydrate and areas of broad consensus, many controversies remain. Most long term data derive from observational studies, which may be affected by confounding and other methodological problems. Most randomised controlled trials are short, rely on proxy measures, lack blinding, do not control for treatment intensity between dietary groups, and have limited compliance. Additional relevant considerations in effectiveness studies include the behavioural and environmental factors (eg, food availability and affordability) affecting compliance. The resolution of these controversies (summarised in box 1) will require mechanistically oriented feeding studies and long term clinical trials, prospective observational research, and examination of economic and environmental impacts.

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