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REVIEW

Optimal dietary approaches for prevention of type 2 diabetes: a life-course perspective

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Abstract In recent years, several alternative dietary approaches, including high-protein and low-glycaemic-load diets, have produced faster rates of weight loss than traditional low-fat, high-carbohydrate diets. These diets share an under-recognised unifying mechanism: the reduction of postprandial glycaemia and insulinaemia. Similarly, some food patterns and specific foods (potatoes, white bread, soft drinks) characterised by hyperglycaemia are associated with higher risk of adiposity and type 2 diabetes. Profound compensatory hyperinsulinaemia, exacerbated by overweight, occurs during critical periods of physiological insulin resistance such as pregnancy and puberty. The dramatic rise in gestational diabetes and type 2 diabetes in the young may therefore be traced to food patterns that exaggerate postprandial glycaemia and insulinaemia. The dietary strategy with the strongest evidence of being able to prevent type 2 diabetes is not the accepted low-fat, high-carbohydrate diet, but alternative dietary approaches that reduce postprandial glycaemia and insulinaemia without adversely affecting other risk factors.

Keywords Diet · Glycaemia · Insulinaemia · Obesity · Review · Type 2 diabetes

Abbreviations

GI	Glycaemic index
GL	Glycaemic load
NAFLD	Non-alcoholic fatty liver disease

Introduction

At the start of this millennium, two large landmark studies showed that dietary intervention can prevent progression from impaired glucose tolerance to overt

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type 2 diabetes [1, 2]. Both studies employed low-fat, high-carbohydrate diets (up to 30% of energy from fat, 10% from saturated fat) combined with physical activity to achieve weight loss. The findings have since been perceived as irrefutable evidence that low-fat, high-carbohydrate diets are the cornerstone for preventing type 2 diabetes among people at risk. In fact, these studies employed integrated diet, physical activity and lifestyle modifications, which resulted in weight loss. As such, the observed benefits cannot be directly attributed to the composition of the diet.

With regard to weight loss, several recent meta-analyses and reviews have concluded that low-carbohydrate, high-protein diets [3–5] and low-glycaemic-index (GI) or low-glycaemic-load (GL) diets [6, 7] may be more successful (or just as effective) as traditional low-fat, high-carbohydrate diets. Indeed, a high-fat Mediterranean-style diet was recently found to be more effective than a low-fat diet over a 2 year period [8]. Over the longer term, some studies suggest that these alternative dietary approaches are more effective for weight loss maintenance than low-fat, high-carbohydrate diets [8–11]. Although the differences may be considered 'modest', small increments in weight over time produce obesity, the single biggest modifiable risk factor for type 2 diabetes. In virtually all studies, alternative dietary approaches have been reported to be more effective than a conventional low-fat diet in optimising the cardiovascular outcomes of weight loss (e.g. improving dyslipidaemia) [5–7]. Taken together, this evidence argues that low-fat diets should not be the preferred dietary approach for persons at risk of developing diabetes.

The present review proposes that all alternative dietary approaches for preventing type 2 diabetes share an under-recognised unifying mechanism: the reduction of postprandial glycaemia and insulinaemia. In this scenario, any diet that facilitates this reduction will improve glucose and lipid metabolism, and relieve the burden on the beta cell. The least effective (or even most damaging) diet would be one that increased postprandial glycaemia and placed excess demands on beta cell function. These adverse effects are most detrimental for the growing number of individuals with features of the insulin resistance syndrome. Certain periods of life, including pregnancy and puberty, are also characterised by physiological insulin resistance [12, 13]. In line with the 'early origins of health and disease' hypothesis, excessive postprandial glycaemia and insulinaemia during these critical windows could program a higher lifetime risk of developing obesity and type 2 diabetes.

Carbohydrates, obesity and diabetes

Since large-scale intervention studies analysing the impact of single dietary modifications on the risk of type 2 diabetes are not feasible, observational studies remain a major source of evidence for differential effects of carbohydrate quantity and quality on risk of type 2 diabetes. Epidemiological studies can be seen as 'natural experiments', but are hampered: (1) by the fact that selective under-reporting of nutritional intake may be related to the degree of overweight, which is the main modifiable risk factor for type 2 diabetes; and (2) by the conscious awareness of the relation between food intake and body weight, i.e. many overweight people are likely to under-report their food intake or to be currently dieting [14]. These limitations are of particular concern for cross-sectional studies on overweight, but less pertinent for prospective studies addressing disease outcomes such as type 2 diabetes. Due to the close alliance of obesity and type 2 diabetes, it nonetheless seems prudent to simultaneously consider the prospective epidemiological evidence linking diet to the subsequent development of both conditions.

Observational studies in adults almost unanimously suggest that high intakes of dietary fibre are effective in reducing the risk of obesity [15–17] and type 2 diabetes [18]. Recent studies focusing on whole grains in place of fibre, show similar benefits [19]. Unfortunately, high intakes of fibre or whole grains may also be markers of a healthier lifestyle [15]. In contrast, the epidemiological evidence for a role of dietary carbohydrate in the development of overweight or type 2 diabetes is much less consistent (see Textbox: Quantity and quality of dietary carbohydrate intake in association with risk of overweight and type 2 diabetes).

In most [17, 20–23], but not all studies [24], intakes of total carbohydrate (whether high or low) were not independently related to the development of obesity or type 2 diabetes. It is thus intriguing to consider that other components of total carbohydrate intake may be counteracting the benefits of a higher fibre intake. High-carbohydrate choices vary considerably, not only in their content of dietary fibre or whole grains, but also in their 'glycaemic potency', i.e. the extent to which the available carbohydrate of a food exaggerates postprandial blood glucose excursions. The GI (a system of ranking foods for this purpose) is calculated as the blood glucose response to a 50 g (or 25 g) carbohydrate portion of food, expressed as a percentage of the same amount of carbohydrate from a reference food, either glucose or white bread [25]. Glycaemic load (GL = quantity of carbohydrate ×

Quantity and quality of dietary carbohydrate intake in association with risk of overweight and type 2 diabetes

Dietary factor	Level of evidence[a] for an association with		Methodological considerations[b]
	Risk of overweight[b]	Risk of type 2 diabetes	
Total carbohydrate intake	↔ [17, 20]	↔ [21–24]	
Dietary fibre	↓↓ [15–17]	↓↓↓ [18]	• May be particularly prone to residual confounding by lifestyle or socioeconomic factors, which epidemiological studies cannot fully control for • Fibre-specific over-reporting cannot be precluded
Whole grain intake	↓↓ [15, 16]	↓↓ [19]	• May be particularly prone to residual confounding by lifestyle or socioeconomic factors, which epidemiological studies cannot fully control for • Definition of wholegrain product varies between studies Ascertainment of whole-grain content is difficult • Whole grain-specific over-reporting cannot be precluded
High GI/GL	↑ [20, 29]	↑↑↑ [22, 23, 26]	• Dietary assessment methods generally not designed to determine GI/GL. In some studies the validity for GI/GL may hence be very low • Residual confounding by lifestyle related factors less likely • GI/GL specific under-reporting unlikely
Western food pattern[c]	↑↑ [36, 37]	↑↑ [31–35]	• Food pattern depend on the population they were derived from • Specific under-reporting of these socially less desirable foods cannot be precluded • Identifiable food groups are determined by the dietary assessment tool (mostly FFQ) used

[a] ↔ Probable evidence of no effect according to several prospective cohort studies
↓↓ Probable evidence of a decreased risk according to several prospective cohort studies
↓↓↓ Convincing evidence of a decreased risk according to several studies including a meta-analysis
↑ Possible evidence of an increased risk according to few prospective cohort studies
↑↑ Probable evidence of an increased risk according to several prospective cohort studies
↑↑↑ Convincing evidence of an increased risk according to several studies including a meta-analysis
[b] See text for general methodological considerations regarding evidence for overweight development
[c] White bread, French fries, mashed/baked potatoes

GI) has been proposed as a global indicator of the overall glucose response induced by a serving of a given food [21].

In a recent meta-analysis, GI and GL showed a clear relationship to the risk of type 2 diabetes [26], even though individual studies may not have shown significance [27, 28]. Interestingly, in some studies, the highest relative risks (>2) were observed among persons with a higher dietary GI or GL, and lower (cereal) fibre intake [22, 23]. Similarly, a higher dietary GI may be associated with subsequent adverse changes in BMI [20] or body weight, as well as body fat percentage and waist [20, 29], although only two studies have addressed this prospectively in adults [20, 29] (see Textbox: Quantity and quality of dietary carbohydrate intake in association with risk of overweight and type 2 diabetes).

Importantly, dietary GI or GL is not prone to confounding in the same way as fibre or whole grain intake. In fact, the tendency of many whole grains to have a high GI [30] works against a significant bias in the observed associations of GI with health outcomes.

Recent prospective studies have used exploratory (rather than hypothesis-based) dietary pattern analyses to identify food choices associated with the risk of developing type 2 diabetes or obesity. Although the identified patterns depend on the population from which they were derived, they are nevertheless similar, showing that increased risk of type 2 diabetes and overweight is associated with higher consumption of refined grains or white bread, ready-to-eat breakfast cereals, sugar-sweetened beverages, potatoes or French fries, and sweets or sweet bakery products; they also show a protective effect on the risk of these two conditions

from other frequent carbohydrate choices such as fruits, vegetables, legumes, whole-meal or whole-grain bread and high-fibre breakfast cereals [31–37].

This body of evidence has contributed to recent public health initiatives directed at reducing soft drink consumption. However, such measures may need to be applied more broadly, since the adverse health consequences observed in dietary pattern analyses are likely to result from the combined effects of unfavourable carbohydrate choices, rather than from any single carbohydrate-providing food group. In fact, the choices associated with an increased risk of developing type 2 diabetes and overweight are generally known to yield higher postprandial glucose and insulin spikes, whereas those associated with a lower risk elicit lower postprandial responses [30].

Carbohydrates and appetite

In the traditional satiety hierarchy, protein is more satiating than carbohydrate and carbohydrate more satiating than fat. Part of the rationale for high-protein diets and high-carbohydrate diets as a means of weight loss is their ability to promote satiety and reduce total energy consumption [38, 39]. However, when appearance, fibre and other factors are controlled for, more slowly digested, low-GI carbohydrate foods have been found to be more satiating than rapidly digested, high-GI carbohydrates [40], eliciting higher levels of satiety hormones such as cholecystokin [41]. An alternative hypothesis is that high postprandial glycaemia is followed by a 'dynamic decline' to levels below baseline in the following hours. This 'reactive hypoglycaemia' has been shown to increase hunger and may lead to a higher subsequent energy intake [42, 43]. The counter-regulatory hormone response to restore euglycaemia also triggers an elevation of NEFA levels [43]. Higher ambient insulin levels may also reduce the oxidation of fat at rest and during exercise [44]. Hence, over the longer term, regular consumption of foods with a high GI may result in a shift from fat to glucose as the preferred metabolic fuel [45]. Resting energy expenditure is also lowered substantially on a low-fat, high-carbohydrate weight loss diet, while a low-GL diet lowers resting energy expenditure to a lesser degree [46].

In the context of conventional low-fat, high-carbohydrate diet, advice usually focuses on the use of fibre-rich foods without reference to their GI. However, most wholemeal breads and many 'wholegrain' flaked breakfast cereals also have a relatively high GI [30]. Thus, even if high fibre intake is achieved, such diets may produce higher day-long glycaemic and insulin profiles than high-fat or low-GI alternatives [47]. Traditional Mediterranean-type diets (characterised by higher fat and lower carbohydrate content), as well as low-carbohydrate and high-protein diets also reduce postprandial glycaemic and/or insulinaemic responses. This occurs despite the fact that these dietary approaches are not tailored specifically to affect postprandial metabolic responses [47–51]. It is thus conceivable that their higher effectiveness is partly attributable to metabolic adaptations similar to those seen on a low-GI or low-GL diet (Fig. 1).

Carbohydrates and glucose homeostasis

Glucose homeostasis plays a major role in the prevention of type 2 diabetes, weight gain and cardiovascular disease. In the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM) trial, treatment with the α-glucosidase inhibitor acarbose, a compound that specifically reduces postprandial hyperglycaemia, reduced the risk of type 2 diabetes [52], weight gain over time [52, 53] and cardiovascular disease [53]. The repeated challenge to glucose homeostasis induced by a low-fat, high-carbohydrate diet is of concern. Healthy, active individuals may adjust to the postprandial glucose challenge following a high-carbohydrate meal (commonly characterised as having a high GI) by increasing the insulin sensitivity of their peripheral tissues [54]. However, less active individuals must increase their insulin secretion in order to re-establish glucose homeostasis. In

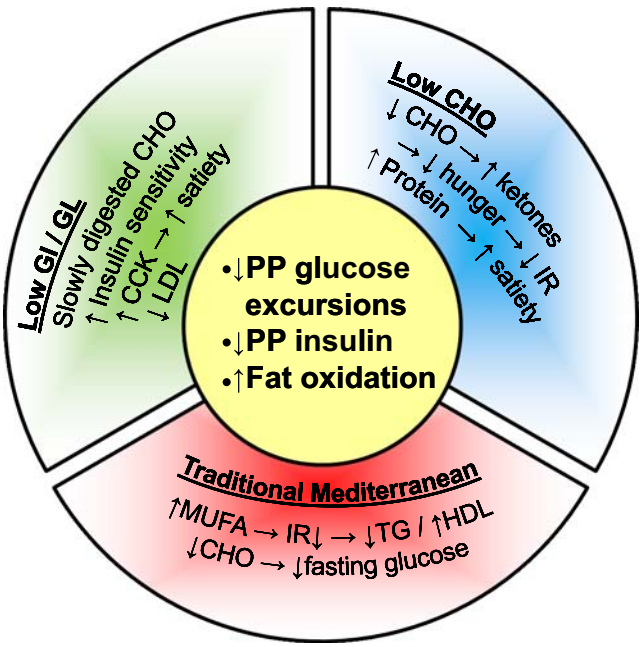

Fig. 1 Mechanisms of three popular alternative dietary strategies potentially relevant to the prevention of overweight and type 2 diabetes. Yellow shaded areas denote the proposed unifying mechanisms. CCK, cholecystokinin; CHO, carbohydrate; IR, insulin resistance; MUFA, monounsaturated fat; PP, postprandial; TG, triacylglycerol

these people, adherence to the recommended high-carbohydrate diet may result in higher postprandial glycaemic and insulinaemic excursions and greater demands on beta cell function, which could eventually promote a more rapid development of type 2 diabetes (Fig. 2) and thereby an increased risk of other adverse health outcomes. In fact, compensatory hyperinsulinaemia when necessary to maintain the metabolic effects of insulin will also lead to an overstimulation of its nuclear effects, hence contributing to the progression of atherosclerosis and development of cancer [55].

Indeed, recent weight loss studies suggest that glucose-tolerant persons with lower insulin secretion can successfully lose weight on either a low-fat, high-carbohydrate diet or an alternative dietary approach, whereas those who present with higher insulin secretion, i.e. those who may be insulin-resistant but still have good beta cell function are much more successful with dietary approaches targeting the reduction of postprandial glycaemia or insulinaemia, i.e. low-GI or GL diets [56, 57]. Animal studies also support the notion that the higher insulin secretion induced by high-GI starch is associated with greater weight gain and disruption of beta cell architecture, while low-GI starch provides benefits [58].

Similarly, evidence for a greater effectiveness among more insulin-resistant persons is also evolving for other alternative dietary approaches. Among overweight, insulin-resistant women, a high-protein diet was more successful in substantially improving waist circumference, and triacylglycerols and insulin levels, over 12 months than a high-carbohydrate diet [10]. In a large recent 2 year workplace trial, a Mediterranean-style diet produced not only more sustained weight loss in all participants than a low-fat, high-carbohydrate diet, but it also improved the fasting plasma glucose and insulin levels more favourably among persons with type 2 diabetes [8]. For patients with type 2 diabetes, a 6 month low-GI diet resulted in moderately lower HbA_{1c} levels, increased HDL-cholesterol levels and a tendency towards a higher body weight reduction than a high cereal fibre diet [59].

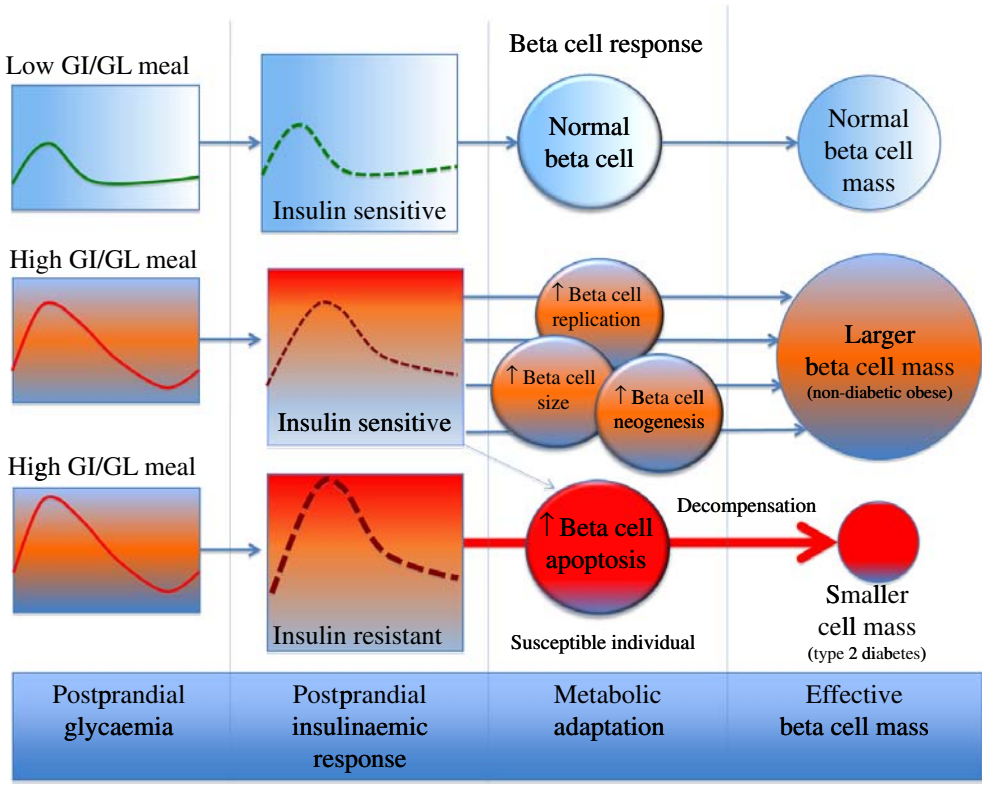

Fig. 2 A tenuous balance exists between insulin resistance and an effective beta cell mass. For the most part, beta cell mass adapts adequately to compensate for changes in the metabolic load. However, beta cells can be pushed too far in susceptible individuals. High-GI carbohydrates and high-GI diets can worsen insulin resistance and contribute to an overwhelming metabolic load. Eventually the beta cell mass fails to compensate for insulin resistance and type 2 diabetes ensues. This failure may be caused by a marked increase in beta cell apoptosis, probably induced by a combination of chronic postprandial hyperglycaemia and hyperlipidaemia, and/or certain cytokines that interfere with the signalling pathways that maintain normal beta cell growth and survival. Of all tissues, the beta cells in particular are especially sensitive to endoplasmic reticulum stress and to oxidative stress caused by high throughput through the mitochondrial chain. The net effect is a reduction in functional beta cell mass in the type 2 diabetic state. Information drawn from previously published work [119, 120]

Carbohydrates, serum lipids and hepatic lipogenesis

There is concern that certain alternative dietary approaches have adverse effects on LDL-cholesterol levels and could therefore increase cardiovascular disease risk over the longer term. In fact, according to a meta-analysis of five weight loss trials, unrestricted low-carbohydrate diets produce more favourable changes in triacylglycerol and HDL-cholesterol than low-fat energy-restricted diets, but tend to increase LDL-cholesterol [5]. Since then, three large-scale weight loss interventions have confirmed the long-term benefits of alternative approaches for triacylglycerol and HDL-cholesterol levels [8, 9, 60]. Sustained adverse effects on LDL-cholesterol were observed in only one trial [60].

With regard to high-protein diets, two recent weight loss trials reported reductions in triacylglycerol levels, which were not accompanied by increases in LDL-cholesterol when carbohydrates were selected from low-GI foods [10, 51]. This observation is in line with a meta-analysis of six weight loss interventions, which reported lower LDL-cholesterol levels under unrestricted low-GI/GL diets when compared with conventional energy-restricted low-fat diets [7]. Furthermore, a meta-regression of 32 intervention trials revealed that reduced fasting triacylglycerol was related to reductions in GL after adjustment for total fat intake [6]. Similarly, beneficial effects on serum triacylglycerol, HDL-cholesterol and LDL-cholesterol levels were found in a meta-analysis of 60 studies analysing the replacement of carbohydrate by mono-unsaturated fat [61]. These broad benefits were recently confirmed in a 2-year intervention using a Mediterranean-style diet in patients with the metabolic syndrome [62].

Favourable effects of all alternative dietary strategies on the atherogenic dyslipidaemia commonly associated with the metabolic syndrome, i.e. on triacylglycerol and HDL-cholesterol, may also extend to the prevention of hepatic fat accumulation [63]. Non-alcoholic fatty liver disease (NAFLD) is increasingly recognised as a co-morbid condition in the pathogenesis of type 2 diabetes mellitus [64]. Although multiple mechanisms are involved, chronic hyperglycaemia and hyperinsulinaemia are considered to play a key role, leading to enhanced glucose uptake by the liver, where glucose is converted to triacylglycerol via de novo lipogenesis, and contributing to excessive lipid storage [64]. In insulin resistance, dietary strategies causing marked postprandial elevations of blood glucose and NEFA could thus contribute to excessive hepatic lipogenesis [63]. In fact, in a cross-sectional evaluation of healthy middle-aged Italians, high-GI dietary habits were associated with high-grade liver steatosis, particularly in insulin-resistant participants [65]. In a 6 month intervention trial, a low-carbohydrate ketogenic diet resulted in a better lipid profile and clearly improved steatosis and inflammation in liver biopsies in comparison to a conventional low-fat diet [66]. Finally, a post hoc analysis of a 1 year weight loss trial conducted in middle-aged obese Israeli patients with type 2 diabetes indicated that a Mediterranean diet reduced alanine aminotransferase levels (a biomarker for NAFLD) to a larger extent than a conventional low-fat diet [67].

Carbohydrates, oxidative stress, inflammation and haemostasis

Oxidative stress, inflammation and haemostasis are emerging risk factors for the development of type 2 diabetes. Some evidence suggests that insulin resistance is a protective mechanism, which is an appropriate cellular response to nutrient excess and overproduction of mitochondrial superoxide [68]. Recurrent hyperglycaemia results in overproduction of reactive free radical molecules and release of pro-inflammatory cytokines, which may in turn induce chronic low-grade inflammation, vascular damage and haemostasis. Naturally occurring antioxidants in food are able to counterbalance the acute and chronic effects of hyperglycaemia and high concentrations of NEFA [69]. Hence, dietary approaches that simultaneously reduce postprandial glycaemia and NEFA levels while contributing to the body's antioxidant defence mechanism could be expected to reduce the likelihood of inflammation.

Indeed, dietary GI influences inflammatory markers acutely and over the long term. In ten lean healthy individuals, nuclear factor-kappa-B activation and nitrotyrosine were substantially reduced in the 3 h following a low-GI breakfast, by comparison with a high-GI meal [70]. Further, low-GI diets were associated with reduced chronic inflammation in recent observational studies [71, 72] and long-term consumption of a diet low in GL resulted in significantly lower levels of high-sensitive C-reactive protein in healthy overweight adults [57].

Similar benefits were observed with Mediterranean-type diets: greater adherence was associated with lower levels of inflammatory [73] and oxidative stress markers [74]. In a two year randomised trial among persons at risk of type 2 diabetes, consumption of a Mediterranean-style diet resulted in a concurrent reduction of inflammatory markers and insulin resistance [62].

Finally, the effects of oxidative stress on haemostasis may be relevant to the development of type 2 diabetes. Four high-quality, randomised controlled trials provide direct evidence that diets with a low GI improve fibrinolysis independently of changes in weight or macronutrient composition [75–78]. Using a parallel study design,

Ebbeling et al. [75] compared an unrestricted low-GL diet with a conventional low-fat diet in 23 obese young adults over 12 months. Thrombogenic potential as measured by plasminogen activator inhibitor-1 concentrations decreased (−39.0%) in the experimental diet group, but increased (33.1%) in the conventional diet group. Changes in weight, cholesterol concentrations, blood pressure and insulin sensitivity did not differ significantly between the groups.

Early origins of obesity and diabetes

Many adult-onset diseases including overweight and type 2 diabetes appear to have their origins in early life. Nutritional programming of diseases with later onset has been defined as 'the idea that stimuli or insults applied during critical or sensitive periods of early life can have lifetime consequences' [79]. Early life, i.e. from conception to late gestation and early postnatal life, is thought to be particularly critical for the development of overweight and type 2 diabetes in later life [79–81]. In addition, the periodicity of the adiposity rebound (~ age 4–6 years, describing the nadir in the BMI growth curve before its continuous rise until adulthood) and adolescence have also been proposed as potentially critical periods for the development of later obesity [82].

Pregnancy and puberty are two potentially critical periods characterised by the development of a physiological insulin resistance. In the second and third trimester of pregnancy, both basal and postprandial insulin levels progressively increase. By the third trimester, basal glucose concentrations are lower, but postprandial glucose levels are elevated and remain elevated for longer. Maternal hepatic glucose production is also increased. This insulin resistance in part serves to re-direct glucose and nutrients away from maternal tissues to the fetus [12]. Puberty in turn is characterised by physiological insulin resistance due to a decrease in insulin sensitivity [13]. It is intriguing that dietary approaches tailored to reducing postprandial glycaemia and insulinaemia could be of particular relevance in these critical windows of time.

Since the Barker hypothesis was first formulated [83], much attention has been given to the observation that low birthweight predisposes to later insulin resistance as well as an increased risk of type 2 diabetes [84]. However, most children now born in developed countries do not have low birthweight. In fact, recent studies indicate a secular increase in birthweight and an accompanying increase in the number of children born large-for-gestational-age or macrosomic (birthweight >4,000 g) [85, 86]. This phenomenon has been attributed in part to increasing prevalence of gestational diabetes and pre-existing diabetes, and/or higher maternal pre-pregnancy BMI [85, 86]. The increasing prevalence of gestational diabetes parallels that of obesity and type 2 diabetes [87]. Offspring exposed to maternal impaired glucose tolerance, diabetes or obesity in utero also have a higher risk of developing overweight or diabetes in later life [80, 81].

Observational evidence for a role of carbohydrate intake in the development of gestational glucose intolerance is emerging, though still controversial [88, 89]. One study found that higher GL and lower fibre intake in the pre-pregnancy diet was associated with an increased risk of developing gestational diabetes [88]. In a randomised controlled trial, the use of a low-GI dietary regimen in women diagnosed with gestational diabetes effectively halved the number who needed to use insulin, with no compromise in obstetric or fetal outcomes [90]. A recent meta-analysis of intervention studies on dietary advice in pregnancy to prevent gestational diabetes concluded that while a low-GI diet may be beneficial, more evidence is needed to substantiate this conclusion [91].

The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study reported a strong continuous association of maternal glycaemia with birthweight and neonatal adiposity for maternal glucose levels below those diagnostic of gestational diabetes [92]. In support, the major influence of maternal glycaemia on fetal growth was on adiposity in a contemporary UK birth cohort [81]. Dietary and lifestyle approaches to reduce glycaemia in all pregnant women are now recognised to be of paramount importance for both mother and child [81, 92]. Intervention studies in women without gestational diabetes suggest that a low-GI diet consumed during pregnancy will reduce the risk of a large infant [93, 94].

Puberty and adolescence

Both absolute and relative carbohydrate intake by adolescents has increased in Western countries [95, 96]. Since this increase has been characterised by higher consumption of carbohydrate choices from refined grains [95] and added sugars or sweets [96] without concomitant increases in fibre intakes [97], it can be assumed that the dietary GL has also increased [98]. With the development of puberty, the quality of dietary carbohydrate may deteriorate further, since adolescents generally consume more fast food and soft drinks than younger children [99]. While these secular and age changes may be well tolerated by normal-weight and physically active adolescents, they are likely to exacerbate the metabolic changes occurring during puberty among those entering adolescence with excess body weight and/or insulin

resistance [100]. For example, in a recent study of healthy German adolescents, a higher dietary GI was associated with adverse changes in body composition only among those who were already overweight when they entered puberty [101].

Insulin sensitivity decreases during mid-puberty, but recovers to pre-pubertal levels by late puberty [100]. This physiological fall in insulin sensitivity during puberty is not related to body fat content [100] and is characterised by a decrease in peripheral insulin sensitivity and higher levels of fasting glucose and insulin, while increases in the acute insulin response are disproportionally low, i.e. the beta cells do not fully adapt to the decrease in insulin sensitivity [13]. Adolescents who require greater acute insulin responses to maintain their glucose tolerance (e.g. obese African-American adolescents) [102, 103] are at higher risk of developing type 2 diabetes [102] over a shorter timeframe than is commonly observed in adults [100]. In this context, a low-fat, high-carbohydrate diet, which induces disproportional insulin spikes, may be an inappropriate choice. Further, increased deposition of NEFAs in intramyocellular compartments is considered partly responsible for the pronounced insulin resistance observed in obese adolescents with impaired glucose tolerance [103]. In this risk population, a dietary regimen that favours 'reactive hypoglycaemia' will subsequently lead to an increase in circulating NEFA, perpetuating a vicious cycle that may eventually precipitate type 2 diabetes.

A low-fat, high-carbohydrate diet may not be harmful during some stages of life and/or metabolic conditions. Specifically, the metabolism of healthy normal-weight children [54] or the metabolism of physically active, insulin-sensitive individuals at most stages of life will probably be able to accommodate large carbohydrate challenges. However, as long-term eating habits are shaped during childhood, dietary advice for children and adolescents should consider the long-term health implications.

The long-term perspective

The search for optimal dietary strategies for prevention of type 2 diabetes should also encompass the need for maintenance of health and primary prevention of other chronic diseases. Ideally, these diets will suit metabolically healthy individuals, prevent progression to disease in those with sub-clinical metabolic derangements and be an optimal treatment for those with overt disease. Studies investigating the long-term effects of different dietary approaches on chronic diseases and all-cause mortality rates are beginning to emerge (see Textbox: Advantages and limitations of common dietary strategies to prevent overweight or type 2 diabetes).

At present, the consumption of low-carbohydrate, high animal protein diets has been associated with increased risk of mortality over the long-term in three observational studies [104–106]. Furthermore, their relatively low fibre content suggests that the risk for some types of cancer may be increased [107]. Thus, caution is required.

Conversely, adverse effects have not been reported for the long-term consumption of Mediterranean-type diets, low-GI/GL diets or low-carbohydrate, high vegetable protein diets. Instead, protection against cardiovascular disease is well established for Mediterranean-type diets [108]. Similar benefits are suggested for low-GI or GL diets [25, 26] and more recently also for high vegetable protein diets [109]. In addition, evidence is emerging that Mediterranean-type diets and low-GI or GL diets also offer modest protection against some cancers [26, 107, 110]. Greater adherence to the traditional Mediterranean diet is associated with a significant reduction in total mortality rates [111, 112]. Future studies will need to address the long-term safety of low-carbohydrate, high vegetable protein diets.

Implementation: individualised dietary advice or public health approaches

For the reasons outlined, a low-fat, high-carbohydrate diet may contribute to a vicious cycle particularly among those who have a genetic or programmed tendency to be insulin-resistant, i.e. individuals with the metabolic syndrome, pregnant women and obese adolescents. Thus, in clinical practice, advice on healthy Mediterranean-style diets or low-GI/GL diets might be considered appropriate for those who would benefit most by preventing or delaying onset of gestational or type 2 diabetes. While physically active, insulin-sensitive individuals are less likely to benefit, the majority of middle-aged and older age groups are not sufficiently active and show a high prevalence of the metabolic syndrome and pre-diabetes. In view of the fact that adherence to healthy Mediterranean-style diets and low-GI/GL diets is not detrimental to the remaining population groups, public health approaches should be considered.

Diabetes prevention beyond the search for optimal dietary approaches

Clearly an optimal dietary approach is only one of the cornerstones of effective prevention of type 2 diabetes. Strategies to address physical inactivity produce similar or additive benefits for risk reduction among those at risk of type 2 diabetes. In the Da Qing Study, interventions to enhance leisure time physical activity with or without a dietary intervention (to increase vegetable intake and to

Advantages and limitations of common dietary strategies to prevent overweight or type 2 diabetes

	Dietary strategies					
	Low-fat high-CHO	Low-CHO (e.g. Atkins)	High-protein, moderate CHO (e.g. Zone)	Low-CHO, high vegetable protein (e.g. ECO-Atkins)	Mediterra-nean	Low GI/GL
Advantages[a]						
Facilitates appropriate intakes of antioxidants, micronutrients and dietary fibre	√			√	√	√
Facilitates low energy density	√					√
Facilitates optimal dietary fat quality				√	√	√
Beneficial effects on LDL-cholesterol	√				√	√
Beneficial effects on HDL-cholesterol and triacylglycerols		√	√	?	√	(√)
Lowers oxidative stress and low-grade inflammation				?	√	√
Lowers risk of cardiovascular disease	(√)	(√)	(√)	√	√	√
Lowers risk of certain cancer types	√				√	√
Allows incorporation of all food groups[b]	√				√	√
Perceived palatability and social desirability may facilitate long-term adherence[b]	√				√	√
Perceived environmental benefits may facilitate long-term adherence[b]	(√)			√	(√)	(√)
Limitations[c]						
Induces postprandial spikes in glycaemia and insulinaemia	√					
Places excess demands on beta cell secretion, may precipitate type 2 diabetes in susceptible individuals	√					
May be associated with a higher mortality risk		√	√			
Long-term effects on kidney function		?	?	?		
Long-term effects on bone metabolism		?	?	?		
References	[107, 117, 118]	[5, 8, 9, 105, 106]	[9, 10, 51, 104–106]	[59, 109]	[61, 62, 73, 74, 107, 108]	[6, 7, 26, 57, 71, 72, 107, 110]

[a] By comparison with a standard Western diet
[b] May vary according to country of origin
[c] For brevity the absence of an advantage is not mentioned as a limitation
CHO, carbohydrate

decrease alcohol and sugar) produced substantial reductions in type 2 diabetes incidence over the 6 year intervention [113]. These benefits were maintained even in the absence of further interventions: each of the three group-based lifestyle interventions (diet, exercise or their combination) produced sustained risk reductions, amounting to a 43% lower overall diabetes incidence in the 20 years of follow-up [114].

Psychosocial stress [115] and effort–reward imbalance [116] are also being increasingly recognised as important risk factors for type 2 diabetes and need to be addressed specifically in future integrated interventions on diet, physical activity and lifestyle.

Conclusions

Clinicians can do better than recommending a conventional low-fat, high-carbohydrate diet for prevention of type 2 diabetes. Most modern high-carbohydrate foods, whether high in fibre or not, place demands on beta cell function and/or insulin sensitivity that threaten glucose homeostasis. Profound compensatory hyperinsulinaemia occurs during periods of physiological insulin resistance such as pregnancy and puberty, and is exacerbated by overweight. The recent rise in gestational diabetes and type 2 diabetes in the young may therefore be traced to food patterns that exaggerate postprandial glycaemia

and insulinaemia. The most evidence-based dietary strategy for prevention of type 2 diabetes includes alternative dietary approaches that reduce postprandial glycaemia and insulinaemia, without adverse effects on other risk factors. Healthy Mediterranean-style diets and low-GI/GL diets could now be recommended in place of conventional low-fat diets.

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Duality of interest J. Brand-Miller is Director of a not-for-profit GI-based food endorsement programme in Australia and manages the University of Sydney GI testing service; she is also co-author of 'The New Glucose Revolution' book series (London: Hodder and Stoughton). All other authors declare that there is no duality of interest associated with this manuscript.

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